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The purpose of this study was to determine the rate of oxygen dilution, resulting from argon accumulation, using 3 low fresh gas flow rates using an oxygen concentrator in a semi-closed anesthesia circle system. This was a prospective, non-experimental descriptive designed study. Nine subjects participated in 3 trials each of fresh gas flows (0.5 liter, 1 liter, and 2 liters) from the oxygen concentrator, with the order counterbalanced, for a total of 27 trials. Preoxygenation and denitrogenation were done prior to the trial beginning. Inspiratory and expiratory gases were measured directly for oxygen, carbon dioxide, and nitrogen; and indirectly for argon. The expiratory gases passed through a carbon dioxide absorber in the circle system prior to entering the inspiratory limb. Continuous monitoring of inspiratory and expiratory gas concentrations was done, including 5 minute recordings. Continuous monitoring of oxygen saturation, respiratory status, and electrocardiogram was done, with 10 minute recordings including blood pressure. A one-way repeated measures ANOVA was used to determine the differences of the inspired oxygen concentration at baseline, 15 minutes, and 30 minutes between subjects for the 3 different flow rates. Data analysis showed a statistically significant difference in inspired oxygen concentration between 0.5 and 1 liter per minute, and between 0.5 and 2 liters per minute. There was not a significant difference between 1 and 2 liters per minute. A statistically significant difference across all three flow rates in inspired concentrations of oxygen ( $p < 0.0001$ ), argon ( $p < 0.0001$ ), and nitrogen ( $p < 0.0001$ ) were seen. There is a statistically and clinically significant increase in oxygen dilution, and argon and nitrogen accumulation at the low flow rate of 0.5 liter per minute. There was no significant difference between 1 liter and 2 liters per minute flow rates in healthy unanesthetized adults, while still assuming a delivery of more than twice the estimated metabolic oxygen requirements. Therefore, this study supports the recommendation of a minimal fresh gas flow rate of 1 liter per minute while using the oxygen concentrator in a semi-closed anesthesia circle systems in healthy adults at rest.

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DETERMINATION OF THE MINIMAL FRESH GAS FLOW TO MAINTAIN A  
THERAPEUTIC INSPIRED OXYGEN CONCENTRATION IN A  
SEMI-CLOSED ANESTHESIA CIRCLE SYSTEM  
USING AN OXYGEN CONCENTRATOR AS  
THE OXYGEN SOURCE

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## Abstract

The purpose of this study was to determine the rate of oxygen dilution, resulting from argon accumulation, using 3 low fresh gas flow rates using an oxygen concentrator in a semi-closed anesthesia circle system. This was a prospective, non-experimental descriptive designed study. Nine subjects participated in 3 trials each of fresh gas flows (0.5 liter, 1 liter, and 2 liters) from the oxygen concentrator, with the order counterbalanced, for a total of 27 trials. Preoxygenation and denitrogenation were done prior to the trial beginning. Inspiratory and expiratory gases were measured directly for oxygen, carbon dioxide, and nitrogen; and indirectly for argon. The expiratory gases passed through a carbon dioxide absorber in the circle system prior to entering the inspiratory limb. Continuous monitoring of inspiratory and expiratory gas concentrations was done, including 5 minute recordings. Continuous monitoring of oxygen saturation, respiratory status, and electrocardiogram was done, with 10 minute recordings including blood pressure. A one-way repeated measures ANOVA was used to determine the differences of the inspired oxygen concentration at baseline, 15 minutes, and 30 minutes between subjects for the 3 different flow rates. Data analysis showed a statistically significant difference in inspired oxygen concentration between 0.5 and 1 liter per minute, and between 0.5 and 2 liters per minute. There was not a significant difference between 1 and 2 liters per minute. A statistically significant difference across all three flow rates in inspired concentrations of oxygen ( $p < 0.0001$ ), argon ( $p < 0.0001$ ), and nitrogen ( $p < 0.0001$ ) were seen. There is a statistically and clinically significant increase in oxygen dilution, and argon and nitrogen accumulation at the low flow rate of 0.5 liter per minute. There was no significant difference between 1 liter and 2 liters per minute flow rates in healthy unanesthetized adults, while still assuming a delivery of more than twice the estimated metabolic oxygen requirements. Therefore, this study supports the recommendation of a minimal fresh gas flow rate of 1 liter per minute while using the oxygen concentrator in a semi-closed anesthesia circle system in healthy adults at rest.

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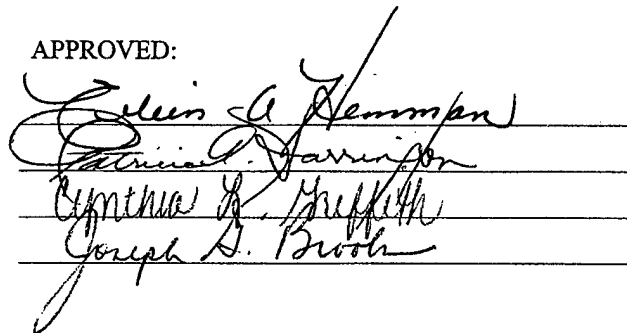
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APPROVED:



# THE UNIVERSITY OF TEXAS



HOUSTON

HEALTH SCIENCE CENTER

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Protection of Human Subjects

## NOTICE OF APPROVAL TO BEGIN RESEARCH

November 17, 2000

HSC-SN-00-022 "Determination of the Minimal Fresh Gas Flow to Maintain a Therapeutic Inspired Oxygen Concentration in a Semi-Closed Anesthesia Circle System using an Oxygen Concentrator as the Oxygen Source"

P.I.: Joan Grano, MSN Student; Andrea Roberts, MSN Student; Annabel Bigley, MSN Student

PROVISIONS: Unless otherwise noted, this approval relates to the research to be conducted under the above referenced title and/or to any associated materials considered at this meeting, e.g. study documents, informed consent, etc.

APPROVED: At a Convened Meeting

APPROVAL DATE: October 20, 2000 EXPIRATION DATE: September 30, 2001

CHAIRPERSON: Anne Dougherty, MD

Subject to any provisions noted above, you may now begin this research.

CHANGES - The P.I. must receive approval from the CPHS before initiating any changes, including those required by the sponsor, which would affect human subjects, e.g. changes in methods or procedures, numbers or kinds of human subjects, or revisions to the informed consent document or procedures. The addition of co-investigators must also receive approval from the CPHS. ALL PROTOCOL REVISIONS MUST BE SUBMITTED TO THE SPONSOR OF THE RESEARCH.

INFORMED CONSENT - Informed consent must be obtained by the P.I. or designee using the format and procedures approved by the CPHS. The P.I. must instruct the designee in the methods approved by the CPHS for the consent process. The individual obtaining informed consent must also sign the consent document.

UNANTICIPATED RISK OR HARM, OR ADVERSE DRUG REACTIONS - The P.I. will immediately inform the CPHS of any unanticipated problems involving risks to subjects or others, of any serious harm to subjects, and of any adverse drug reactions.

RECORDS - The P.I. will maintain adequate records, including signed consent documents if required, in a manner which ensures confidentiality.

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## CHAPTER I

### Introduction

Oxygen concentrators have gained popularity in field military hospitals. They are currently being used by Forward Surgical Teams in the field medical environment, specifically with the draw-over anesthesia system because they are a safe, inexpensive alternative to oxygen cylinders. Oxygen concentrators produce an unlimited supply of oxygen, which solves the logistical problems associated with deployed oxygen supplies, and replaces the compressed oxygen cylinders. The draw-over anesthesia system uses an open system where gases are not recirculated. The rate of oxygen dilution resulting from argon accumulation in a semi-closed anesthesia circle system at low flow rates is unknown. To use this system efficiently and safely in anesthesia, there is a need to determine which flow rates can be used in a semi-closed anesthesia circle system while using the oxygen concentrator as the oxygen source. Once this flow rate is determined, this information can be used in future research with oxygen concentrators configured to a field anesthesia machine to give oxygen to anesthetized patients.

Oxygen concentrators produce  $93\% \pm 3\%$  oxygen (Friesen, 1992) and less than 1% nitrogen. The remaining gas is assumed to be argon. When using an oxygen concentrator with a semi-closed anesthesia circle system, there is an accumulation of argon and nitrogen within the circuit during low flow delivery of fresh gas (Parker & Snowdon, 1988). During high fresh gas flow, these additional gases do not usually accumulate because they are vented outside the circuit by the adjustable pressure limiting (APL) valve. During low fresh gas flows, the metabolic consumption of oxygen may approach equilibrium with the fresh gas flow. The exhaled gases that are not vented begin to accumulate within the semi-closed circuit. When the fresh gas flow rate delivered from the oxygen concentrator to the semi-closed anesthesia circle system decreases, argon and nitrogen accumulate. This decreases the available oxygen concentration in the inspiratory circuit (Barash, Cullen, & Stoelting, 1997).

#### Statement of the Problem

Oxygen dilution occurs as argon accumulates within a semi-closed anesthesia circle system at low flow rates, when using an oxygen concentrator as the oxygen source (Parker & Snowden, 1988). If argon continually displaces oxygen in the circuit, it is possible that the patient may receive a gas mixture that

contains less than 21% oxygen. Therefore, it is critical to show the effects of the different flow rates from the oxygen concentrator on the inspired oxygen concentration while using the semi-closed anesthesia circle system in an unanesthetized subject while maintaining an inspired oxygen level above 21%. This study will determine the rate of oxygen dilution, resulting from argon accumulation, using three different flow rates from an oxygen concentrator in a semi-closed anesthesia circle system.

### Theoretical Framework

A physiological model using Dalton's Law of partial pressures will serve as the conceptual framework for this study. According to Dalton's Law, the pressure exerted by each individual gas in a gas mixture is independent of the pressures of the other gases (Levitzky, 1999). The partial pressure of respiratory gases in the alveoli is determined by their concentration in inspired air and the metabolic consumption of oxygen and the production of carbon dioxide in the body. The partial pressure of a particular gas in the mixture is equal to the total pressure of all the gases times the fractional concentration of the particular gas. Oxygen comprises 21% of atmospheric air; therefore at standard barometric pressure of 760 mmHg, oxygen has a partial pressure of 159.6 mmHg. In contrast, carbon dioxide comprises 0.04% of atmospheric air with a partial pressure of 0.3 mmHg.

Oxygen is brought into the lungs from the atmosphere to the alveoli during inspiration. Carbon dioxide is carried out of the lungs during exhalation. A volume of fresh air enters the alveoli per minute, and a similar volume leaves. The actual volume of gases entering and leaving the alveoli per minute depends on the volume of the lungs, mechanics of the chest wall, the muscles of inspiration and expiration, and the rate of breathing. Pathological or physiological conditions may alter these factors and influence alveolar ventilation.

Metabolic processes of the body determine the levels of oxygen consumption and carbon dioxide production. During the resting respiratory cycle, alveolar ventilation occurs where approximately 250cc of carbon dioxide per minute diffuse from the pulmonary capillary blood into the alveoli in exchange for about 300cc of oxygen. The metabolic rate of oxygen consumption is 3.4 milliliters per kilogram per minute (Levitzky, 1999).

As air is inspired, it is heated and humidified by the respiratory system with the addition of warm water vapor. The partial pressure of water vapor is added to the mixture. At normal body temperature, the partial pressure of water vapor is 47 mmHg (Levitzky, 1999). The partial pressure of inspired alveolar oxygen ( $P_{AO_2}$ ) is 149 mmHg when water vapor is added. At sea level, this is the highest partial pressure of alveolar oxygen that can be achieved without adding supplemental oxygen. So even with an increase in alveolar ventilation, a higher partial pressure of alveolar oxygen will not be achieved (Levitzky, 1999).

The partial pressure gradient of each gas across the alveolar-capillary membrane is a major factor in the rate of diffusion. Alveolar-capillary membrane properties and the actual physical properties of a gas will also influence diffusion. The alveolar partial pressure of each gas is different during inspiration and expiration. On inspiration, it is dependent on the concentration of the inspired gas mixture. On expiration, it is dependent on the metabolic consumption of oxygen and the production of carbon dioxide (Levitzky, 1999).

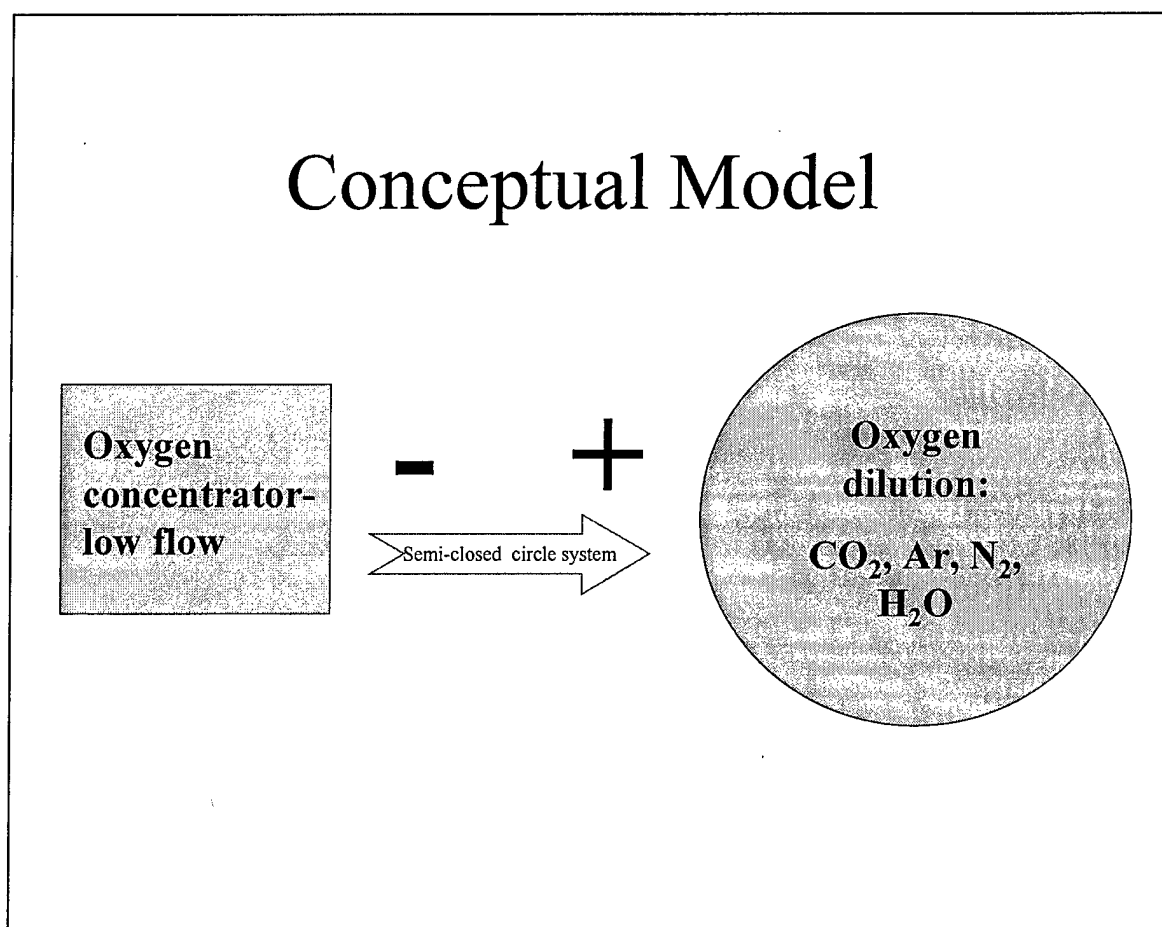
The conceptual model for this study applies Dalton's Law (Figure 1) to the semi-closed anesthesia circle system (Figure 2) and the variations in gas concentrations seen with inspiration and expiration. In this study, the oxygen concentrator supplies a gas mixture of  $93\% \pm 3\%$  oxygen, less than 1% nitrogen, and the remainder concentration being argon. The subject will only breathe this mixture supplied by the oxygen concentrator. Initial elimination of the normal pulmonary nitrogen stores is achieved by first inhaling the fresh gas mixture at a 10 liter per minute flow. A semi-closed system is maintained throughout the trial. The only adjustment will be to the APL valve. The APL valve is a positive and negative pressure relief valve. This valve is adjusted to allow excess gas to vent from the circuit. During the 10 liter flow this valve is opened completely, then it is adjusted depending on the flow rate.

During inspiration, using Dalton's Law, the total pressure of gases in the inspiratory limb include oxygen, argon, and nitrogen. The partial pressure of water vapor is added to this total as the gases are humidified and warmed by the body. During expiration, the total pressure of gases include oxygen, carbon dioxide, water vapor, nitrogen, and argon. Exhaled carbon dioxide is absorbed by an inline carbon dioxide absorber and will not return to the inspiratory side of the circuit. Excess gas in the circuit is released to the atmosphere by the APL valve. The remaining gases return to the inspiratory side of the circuit and will

**Figure 1.** Dalton's Law shows that the partial pressures of all inspired gases are included in the total pressure in the alveoli.

Dalton's Law of Partial Pressures	
$P_A = P_{H_2O} + P_{O_2} + P_{CO_2} + P_{N_2} + P_{Ar}$	
$P_A$ = Total alveolar pressure	$P_{CO_2}$ = Partial pressure of $CO_2$
$P_{H_2O}$ = Partial pressure of $H_2O$	$P_{N_2}$ = Partial pressure of $N_2$
$P_{O_2}$ = Partial pressure of $O_2$	$P_{Ar}$ = Partial pressure of Ar

**Figure 2.** Over time, oxygen is diluted by argon in the semi-closed anesthesia circle system when using an oxygen concentrator.



dilute the concentration of oxygen that is added by the fresh gas flow from the oxygen concentrator. Argon is an inert gas; it is not reabsorbed inline (like carbon dioxide) or metabolized. Argon will return to the inspiratory limb, excess gas will be released by the APL valve or it will begin to accumulate within the circuit. The partial pressure of argon will displace the concentration, thus partial pressure, of oxygen within the inspiratory circuit. The partial pressure of the gases within the inspiratory side of the circuit, thus the inspired oxygen concentration, will be influenced by the fresh gas flow rate.

#### Purpose

The purpose of this study was to determine the rate of oxygen dilution, resulting from argon accumulation, using three different low fresh gas flow rates while using an oxygen concentrator as the fresh gas source in a semi-closed anesthesia circle system.

#### Definition of Terms

Argon. Conceptual definition: A chemically inert gas that is nonflammable, nontoxic, colorless, odorless, and tasteless. It does not form chemical compounds. Room air contains 0.94% argon by volume (Especial Gas, Inc, 2000a). Operational definition: The oxygen concentrator delivers approximately 5% argon. It is measured indirectly by subtracting the concentration of oxygen, carbon dioxide, and nitrogen, which are measured by the Ohmeda Rascal® II Anesthetic Gas Monitor, from 100%. The remaining concentration was assumed to be argon.

Fresh Gas Flow. Conceptual definition: The liter per minute flow added to the breathing circuit (Barash et al., 1997). Operational definition: One-half liter, 1 liter, or 2 liter per minute fresh gas flow from the oxygen concentrator that was delivered to the breathing circuit as measured by the Cole Parmer flow meter. The rate of fresh gas flow was different for each trial. The trials were counterbalanced.

Low Flow Anesthesia. Conceptual definition: Any fresh gas flow rate added to the semi-closed anesthesia circle system that is less than three liters per minute but more than the basal metabolic oxygen demand of the person (Miller, 2000). The basal metabolic oxygen demand is 3.4 milliliters per kilogram per minute (Levitzky, 1999). Operational definition: A maximum fresh gas flow of 2 liters per minute and a minimal fresh gas flow of 0.5 liter per minute, as measured by the Cole Parmer flow meter, was used.

Oxygen Concentrator. Conceptual definition: A machine that produces a high concentration of oxygen by passing atmospheric air through a molecular sieve. This process separates and concentrates the oxygen (Friesen, 1992). Operational definition: The Chad Therapeutics, Total O<sub>2</sub> Delivery System (TO-001), oxygen concentrator was used.

Semi-closed Anesthesia Circle System. Conceptual definition: A breathing circuit, used in providing anesthesia, consisting of inspiratory and expiratory limbs, unidirectional valves, a reservoir, an adjustable pressure limiting valve, and a carbon dioxide absorber configured in a circular fashion. In this system, carbon dioxide is removed from the exhaled gases by a carbon dioxide absorber. The remaining exhaled gases are then returned to the inspiratory limb. Fresh gas is added to remaining exhaled gases in the inspiratory limb for the patient to breathe (Barash et al., 1997). Operational definition: A single use disposable breathing circuit containing inspiratory and expiratory limbs with unidirectional valves by Vital Signs was used. An inline soda lime carbon dioxide absorber, *Iso-Gard Disposable CO<sub>2</sub> Absorber*, which includes an APL valve was included.

Therapeutic FiO<sub>2</sub>. Conceptual definition: Air normally contains 20.9% oxygen, which under normal circumstances, will maintain life (Hardman & Limbird, 1996). Operational definition: An oxygen concentration that was 21%.

### Hypothesis

Research hypothesis: There will be an increase in the rate of oxygen dilution, while remaining above an inspired oxygen concentration of 21%, by argon as flow rates decrease in a semi-closed anesthesia circle system using an oxygen concentrator for the fresh gas source.

Null hypothesis: There will be no difference in the concentration of oxygen delivered to the subject, via the semi-closed anesthesia circle system, at different fresh gas flows when using an oxygen concentrator.

### Significance of the Problem

Oxygen concentrators are currently used in two ways in military field hospitals. They are used to supply oxygen in different patient units and they are used in the draw-over anesthesia system. Oxygen concentrators are a safe, inexpensive alternative to oxygen cylinders in the field medical environment.

In the field environment, low flow anesthesia is a common practice. Any gas that is added to the anesthesia circle system has a potential for diluting the oxygen content. However, this is not an issue in a hospital operating room, since 100% oxygen is the fresh gas source. Safe flow rates using 100% oxygen have long been established. The use of an oxygen concentrator in a semi-closed system changes the system conditions and requires us to investigate safe fresh gas flow rates under these new conditions. To use this oxygen concentrator system efficiently and safely in anesthesia, there is a need to determine a low flow rate in a semi-closed anesthesia circle system that is safe for the patient and efficient in conserving resources. Implications of our research could lead to further research and development of a field anesthesia machine with an oxygen concentrator appropriately configured to deliver oxygen and anesthesia to patients.

#### Assumptions

Below are a list of assumptions that were made for this study.

1. The health history obtained from the subject was accurate.
2. Physiological properties were normally distributed through out this population.
3. Inhalation of a small concentration of argon was not harmful.
4. The oxygen and argon concentration from the oxygen concentrator was consistent.
5. The inspired and expired gases analyzed by the Ohmeda Rascal® II Anesthetic Gas Monitor includes: oxygen, carbon dioxide, and nitrogen. The remaining concentration of gas that is unaccounted for was argon.

#### Limitations

Below are a list of limitations that were made for this study.

1. There were pre-existing differences among subjects related to lung capacities and volumes. The subject's gender, race, height and weight were recorded.
2. Although there was no attrition; attrition from the group could have occurred during the trials because of health changes or by request.
3. The subjects did not receive any anesthesia. Their oxygen metabolic consumption may be higher or lower than a patient who is receiving anesthesia, so our findings do not represent a true clinical anesthetic situation.

4. The subjects were a convenience sample of healthy U. S. Army personnel and therefore generalizability is limited. Demographics were collected to describe the subjects.

5. The Ohmeda Rascal® II Anesthetic Gas Monitor does not measure the water vapor within the circuit. Gas analysis is done with dry gases; therefore the percent of gases measured within the circuit did not include water vapor.

#### Summary

In summary, gas diffusion is influenced by the partial pressure difference of the gas across the alveolar-capillary membrane. Using Dalton's Law of partial pressure, all inspired gases in the gas mixture are independent of the pressures of the other gases in the mixture. Oxygen and carbon dioxide have diffusion capabilities across the alveolar membrane based on their partial pressures and individual gas properties. While using an oxygen concentrator with a semi-closed anesthesia circle system, oxygen, nitrogen, and argon are supplied to the circuit. Although nitrogen concentration is minimal, the literature indicates a potential accumulation during very low flows (Parker & Snowden, 1988). Although water vapor is added to the total pressure, it is removed by the gas analyzer prior to analysis, and in this study, it is assumed to be fairly constant.

This study was done to determine the rate of oxygen dilution while using an oxygen concentrator as the fresh gas source in a semi-closed anesthesia circle system. According to Dalton's Law, as argon and nitrogen accumulate within the circuit during low fresh gas flow delivery, they displace oxygen. As time passes, this decreases the partial pressure of oxygen, thus decreasing the amount of oxygen available for alveolar diffusion.

## CHAPTER II

### Review of Related Literature

Oxygen is a resource for patient care both in hospitals and in home health. Supplemental oxygen is used whenever the patient is unable to maintain a satisfactory oxygen saturation from breathing atmospheric air. Oxygen is given to the patient during surgery because the medications used to induce anesthesia impairs the patient's ability to maintain a satisfactory oxygen saturation from atmospheric air alone (Hall, 1997).

Traditionally, the delivery of oxygen is by the use of oxygen cylinders. Oxygen in the cylinder is under a great deal of pressure and is considered a hazardous material. Oxygen supports combustion. If an oxygen cylinder cracks, falls, or breaks, it can become a deadly projectile. There are also problems with filling oxygen cylinders. If performed incorrectly there is the possibility of contamination or misfilling of the gas in the cylinder. In many countries, there are regulations governing the filling, transportation, and storage of oxygen (Eichhorn & Ehrenwerth, 1993).

Oxygen concentrators were initially designed in the 1960's as an alternative to oxygen cylinders for the home health industry (World Health Organization [WHO], 1993). Oxygen concentrators are used throughout the world to make quality of life better for people dependent on supplemental oxygen. Patients can live a more active life at home with the use of an oxygen concentrator rather than in a hospital bed connected to a central oxygen source.

Oxygen concentrators are small and portable, and are used in places where there is a shortage of compressed oxygen in cylinders. Situations where they are used include: military and disaster situations, developing countries (Wilson, van Heerden, & Leigh, 1990), and where it is too expensive or logistically impractical to bring a large quantity of gas cylinders (Rathgeber, Zuchner, Kietzmann, & Kraus, 1995). Oxygen concentrators provide medical grade oxygen for many other applications as well, such as military mobile hospitals, fighter aircraft, naval vessels, and remote medical facilities around the world (Friesen, 1992).

The difference between using oxygen concentrators for delivery of supplemental oxygen for patients in their home, for pilots in fighter aircraft, and for anesthesia, is the breathing circuit. In the first two

examples, the oxygen from the oxygen concentrator is being delivered at a high fresh gas flow rate in an open system. An open system means that oxygen is breathed in from the concentrator through a nasal cannula or mask, for example, and then exhaled out directly to the atmosphere. For anesthesia delivery, a closed or semi-closed anesthesia circle system is used with lower fresh gas flow rates. This means that most of the exhaled gases, if not released by the APL valve, will stay within the breathing circuit. One complication of using an oxygen concentrator is that it produces oxygen with a small percentage of argon and nitrogen. In a closed system or semi-closed system with low fresh gas flows, argon is not completely allowed to escape to the atmosphere. The potential problem identified with this system is that argon can build up to unacceptable levels in the anesthesia circle system, especially at low fresh gas flows (Parker & Snowden, 1988). There is a potential for nitrogen to buildup in a closed system if inadequate denitrogenation has not occurred (Barash et al., 1997). However, even adequate denitrogenation of 6-8 minutes still cannot guarantee a nitrogen free system (Morita, Latta, Hambro, & Snider, 1985). This chapter reviews literature on oxygen concentrators; medical gases including helium, nitrogen, and argon; argon accumulation; and low flow anesthesia.

### Oxygen Concentrators

According to Friesen (1992), most oxygen concentrators use a molecular sieve design. In this design, air is forced into a chamber containing zeolite (aluminium silicate). Zeolite absorbs nitrogen, thus removing it from the air. Oxygen and any other gases small enough to pass through the zeolite, are collected in another chamber. To maintain a constant oxygen supply there are two zeolite chambers. While air is forced into one chamber, the nitrogen is removed from the other. The gas in the collecting chamber is approximately 93% oxygen. At higher flow rates, oxygen molecules spend less time in the molecular sieve chamber, therefore a lower concentration of oxygen is produced (Gould, Scott, Hayhurst, & Flenley, 1985).

### Advantages

The primary advantages to using oxygen concentrators are cost savings and low maintenance. Dobson (1991) compared the cost of oxygen cylinders to oxygen concentrators in Papua, New Guinea. Spread over 10 years, the oxygen concentrators provided a savings of 25% for smaller rural hospitals and 75% for large district hospitals. Dobson, Peel, & Khallaf (1996), in a different study done in Egypt, looked at

maintenance and cost savings of 22 oxygen concentrators. Dobson et al. (1996) showed that the use of oxygen concentrators with proper maintenance from trained technicians saved enough money to purchase the 22 concentrators within 6 months. After one year, of the 22 oxygen concentrators initially delivered, only one required repair and one was not functioning. The local technician repaired the oxygen concentrator and returned it to service. The oxygen concentrators functioned an averaged of 3,712 hours, producing 18 million liters of oxygen. Both studies concluded that oxygen concentrators are cost effective and have low maintenance requirements.

In the military, oxygen concentrators are very beneficial where transporting heavy oxygen cylinders is logistically and financially problematic, and dangerous. Brock-Utne (1992) and others have noted the success when oxygen concentrators have been used in armed conflicts including Afghanistan (Sogan, Bridel, Shepherd, Arzomand, & Southall, 1998) and Bosnia (Acheson, 1999).

#### Disadvantages

Three disadvantages of oxygen concentrators are the low flow rate, decreased concentration of oxygen produced, and the accumulation of argon in a circle breathing system. First, most oxygen concentrators can only produce a maximum rate of 4 liters per minute. Because of this, low flow anesthesia is a technique that must be employed. Second, oxygen concentrators can only produce a gas with an oxygen concentration greater than 90% if the flow rate is less than 5 liters per minute. At higher flow rates the percent of oxygen concentration produced decreases because air has less time to spend in the zeolite chamber which separates the nitrogen from the oxygen. On one test of an oxygen concentrator at 5 liters per minute, an oxygen concentration of 75% was documented (Fenton, 1989). Lastly, argon accumulates at low fresh gas flow rates in the semi-closed anesthesia circle system. The presence of argon decreases the total percent of oxygen from 100% to between 90% and 96% (Rathgeber et al., 1995).

#### Medical Gases

Air is made up of 78% nitrogen, 21% oxygen, and 1% trace elements or rare gases. The additional elements in air are: water vapor, carbon dioxide, ammonia, argon, helium, neon, krypton, and xenon. Oxygen concentrators work by the use of molecular zeolite sieve technology. Oxygen, nitrogen and argon have molecular diameters that are small enough to pass through the pores of a molecular sieve. This is why

oxygen, nitrogen, and argon are in the product gases. Nitrogen is minimized in the product gas because it is absorbed by zeolite. Argon may or may not be absorbed by the zeolite and some oxygen may be absorbed too (Friesen, 1992). Since argon is a gas that will be delivered with oxygen from the oxygen concentrator, it is important to evaluate the effects of argon accumulation.

Recently, argon has been used in the medical field and for diagnostic tests and research. However, the more commonly discussed gases in the medical field are helium and nitrogen. Because argon is not commonly used and helium possesses similar properties to argon, a review of helium will be helpful in understanding the characteristics and properties of argon. Since nitrogen is also used in the studies of the lung and is an element that may accumulate with the argon, a review of nitrogen will also be discussed.

### Helium

Helium is one of the inert gases in the atmosphere and is commonly used in the medical field. Helium does not accumulate in the molecular sieve and is not one of the product gases from the oxygen concentrator. However, helium is very similar to argon in physical characteristics. Helium is commonly used in the medical field and the effects are not harmful on the lungs. One researcher stated that argon and helium could theoretically be interchangeable in lung studies (Yin, 1989). Since we know how helium acts in the lungs, this will give us a theoretical understanding as to how argon would act in the lungs too.

The atomic weight of helium is 4.0026; it has a density of 0.1785 g/liter; and it is a colorless, odorless, non-reactive, tasteless, and nonflammable gas (Corpbrothers, Inc., 2000b; Especial Gas, Inc., 2000b). Helium is the second lightest element and is only 0.0005% of the atmosphere. It does not form compounds, and its molecules consist of single atoms. However, unlike argon, helium is able to leak gradually out to space. Helium, mixed with oxygen, is used in high pressure breathing systems such as scuba diving. This is feasible because of its low solubility in the blood (Especial Gas, Inc., 2000b).

Helium is commonly seen in the medical field, not for therapeutic application, but for studies and tests involving breathing and measuring lung capacities. For example, Bennett (1965) used helium, nitrogen, and argon to measure cortical carbon dioxide and oxygen levels by breathing mixtures of oxygen and noble gases. Black, Hahn, Maynard, and Scott (1984) used helium, nitrogen, oxygen, and argon to measure lung volumes.

There are other medical applications when helium is mixed with oxygen, also known as heliox (Corpbrothers, Inc., 2000b). Cros, Geunard, and Boudey (1988) report that high frequency jet ventilation with heliox and nitrox, an oxygen and nitrogen mixture, is used during microlaryngeal laser surgery to provide better ventilation and gas exchange with low airway pressures.

Clinically, helium is used frequently in the measurement of functional residual capacity and total lung volume. The subject breathes in a mixture of oxygen and helium to a certain requirement and a calculation is done to derive the total lung volume. This method has been established as a safe way to measure lung volumes.

### Nitrogen

Nitrogen is one of the gases in the atmosphere. It makes up 78% of the volume of the air we breathe (Corpbrothers, Inc., 2000c). Nitrogen has the potential to accumulate in the product gas from the oxygen concentrator. Nitrogen also has some properties that are similar to argon, which like helium, can give us a better insight to argon.

Nitrogen is a colorless, odorless, nontoxic, nonflammable gas. Nitrogen has an atomic weight of 28 (Especial Gas, Inc., 2000c) and a density of 1.250 (Ikels & Adams, 1979). Nitrogen possesses the properties of inert gases. Since our lungs normally contain a large amount of nitrogen, it is clear that nitrogen is safe in the lungs. Nitrogen, like helium, can be used in the measurement of lung volumes. Nitrogen is used in the medical field for tests and studies involving the lungs, which are similar to studies found using helium (Bennett, 1965; Black et al., 1984; Cros et al., 1988). A large amount of research has been done using nitrogen as a wash-out method. Some of which were discussed in the previous section.

Nitrogen is very important to understand in this research study. Nitrogen is mostly separated from the product gas by the oxygen concentrator because of the molecular sieve design. Less than 1% nitrogen should accompany the oxygen. However, about 78% of inspired atmospheric air is nitrogen. In order to determine if nitrogen is accompanying oxygen and argon from the oxygen concentrator, or if there is a leak in the anesthesia circle system, nitrogen must be removed from the subject's lungs by a wash-out method. This wash-out process is called denitrogenation. The subject breathed a 10 liter per minute flow of the product gas stored in a special cylinder tank to eliminate pulmonary nitrogen stores from their lungs prior

to the use of the oxygen concentrator at low flows. This should eliminate any problem with nitrogen buildup in the circuit (Parker & Snowden, 1988).

Barton and Nunn (1975) described the increase in nitrogen concentrations seen in the inspired gas with a closed circuit. Nitrogen concentrations increased faster in subjects who had the shortest periods of denitrogenation. The final concentration of nitrogen ranged from 3.5% to 15% at the end of the anesthetic. The totally closed circuit was primed with 30% oxygen and 70% nitrous oxide. The duration of the closed circuit anesthetic in this study ranged from 34 to 135 minutes. The duration of preoxygenation with an open circuit ranged from 5 to 25 minutes.

Morita et al. (1985) monitored the closed circuit gas accumulation of methane, nitrogen, and acetone during routine anesthesia. The first group of subjects used a high flow semi-closed system for 6 to 8 minutes for denitrogenation. The average nitrogen concentration increased from 6.4% to 16.2% at 120 minutes. The second group of subjects used a high flow semi-closed system for 33 minutes for denitrogenation. The average nitrogen concentration increased from 1.0% to 5.1% at 120 minutes. By increasing the denitrogenation time from 8 to 33 minutes, this lessened the rate at which the nitrogen concentration increased. Flushing the circuit rapidly also decreased the nitrogen level. They hypothesize that with a shorter period of denitrogenation, that nitrogen is probably transported to the lungs from all body tissue compartments. Nitrogen that is in the vessel rich tissues (heart, brain, kidney, and liver) is eliminated rapidly. But the nitrogen that is stored in muscle, fat, and vessel poor tissues (cartilage and bone) is still being eliminated in exhaled air even after 30 minutes of breathing oxygen. This results in accumulation of nitrogen in a closed circuit.

### Argon

Argon, an inert gas, is odorless and colorless. It is the most abundant and industrially used of the inert gases. Argon is 1.3% of the atmosphere by weight (Jackson, 1999) and 0.94% by volume (Especial Gas, Inc., 2000a). Argon's atomic weight is 39.9 and density is 1.784 g/liter. These values are greater than helium and nitrogen. Argon acts as a simple asphyxiant by displacing air. It forms no known chemical compounds (Corpbrothers, Inc., 2000a) and was named from the Greek word "argos" meaning "inactive" (West Point, 2000). Argon's chemical properties are very similar to helium and nitrogen.

Argon was first isolated in 1894 (Jackson, 1999). It was the first of the noble gases to be discovered (Especial Gas, Inc., 2000a). Argon can be found trapped in rocks. It is the product of the disintegration of radioactive isotope potassium-40, which has a half-life of about 12.7 billion years and transforms into argon-40 (Emsley, 1994). The gas slowly leaks from the rocks into the atmosphere and accumulates in large quantities because the earth's gravity prevents it from escaping. (Especial Gas, Inc., 2000a).

Argon has become more popular in research, with an increasing number of researchers choosing argon instead of helium or nitrogen for their studies. Argon has similar properties to its sister gases, helium and nitrogen, which are considered safe and widely used in the medical field. According to Emsley (1994), argon lasers are used to treat tumors and to study the form of oxygen that is theorized to cause skin cancer. In some hospitals, an argon and oxygen mixture is used, instead of or in addition to heliox, to measure lung volumes (Imanaka et al., 1990). Since argon has physical characteristics that favor inert gas wash-in, the use of argon has increased. In addition, argon was a significant part of the respiratory gas mixture in a proposed military aviation respiratory gas generation system (Horrigan, Wells, Guest, Hart, & Goodpasture, 1979).

Argon does have anesthetic properties. However, this does not occur until argon is at 15.2-16.9 atmospheres. On the other hand, oxygen is a potent convulsant at 3 atmospheres and an anesthetic at 5 atmospheres (Friesen, 1992). At low concentrations of argon exposure, there have been no known physiological effects (Friesen, 1992). Argon has a similar viscosity to oxygen but is more dense. When the argon concentration is less than 7%, in the oxygen mixture, it does not alter the flow characteristics of oxygen (Friesen, 1992). Horrigan et al. (1979) demonstrated in an experiment with human subjects breathing 20% oxygen and 80% argon, that argon wash-in mirrors nitrogen wash-out. Since nitrogen is a well-established gas used to measure lung volume by a wash-out method, it seems feasible to rely on results using an argon wash-in method to measure lung volume. Saidel and Lin (1986) discuss the expiratory argon concentration curve from single breath dynamics. When there is a uniform distribution of ventilation and perfusion, there is nearly a horizontal alveolar plateau.

Yin (1989) reported that argon has a distinct advantage over helium because it is about 25 times cheaper than helium in China and more easily available. Yin compared the properties of helium and argon and concluded that helium had a better diffusing capacity than argon, but it was not significantly different. These results indicated that argon can be used instead of helium for the measurement of diffusing capacity in the lungs for carbon monoxide. No additional articles were found indicating the costs of argon and helium in the United States.

However, the relevant point in the discussion of argon, is that the properties of argon are very similar to helium, and argon could theoretically replace helium without adverse effects (Yin, 1989). Establishing a background on argon use and comparing it to the more commonly used gases, helium and nitrogen, establishes the safety of argon in the lungs.

#### Argon Accumulation

Argon has been characterized as a safe gas in the lungs at one atmosphere as long as a hypoxic mixture does not occur. Accumulation of argon in a semi-closed anesthesia circle system is a potential problem when used with the low flows of the oxygen concentrators. An oxygen concentrator produces a maximum oxygen content of approximately 94-95% with 4-5% argon, and less than 1% nitrogen (Parker & Snowdon, 1988; Rathgeber et al., 1995). With an open circuit, argon is inhaled into the lungs with the oxygen and then exhaled into the atmosphere. The person breathing oxygen from an oxygen concentrator in this open system does not get a build up of argon in their lungs or within the breathing circuit. But, in a semi-closed or closed anesthesia circle system, argon can accumulate in the system. The small percentage of nitrogen that accompanies the oxygen from the concentrator should not pose a problem since the subject breathed a 10 liter per minute flow to eliminate pulmonary nitrogen stores from their lungs prior to the use of the oxygen concentrator at low flows. This should eliminate any problem with nitrogen build up (Parker & Snowdon, 1988). With argon, there is a possibility that accumulation can occur in a rebreathing anesthesia system with the use of low fresh gas flow below 0.5 liter per minute from an oxygen concentrator (Parker & Snowdon, 1988; Rathgeber et al., 1995).

Johnson, Swanson, Sodal, Reeves, and Virtue (1979) discussed the concept of lung shrinkage in a closed system that influenced the concentration of gases. Gas uptake is a function of concentration. The

concentration effect seen in this study is related to large volumes of soluble gas uptake in the blood resulting in progressive shrinkage of alveolar volume. The soluble gas concentration in the lung, when the alveolar volume contracts, was maintained at a higher level. This study used nitrous oxide as the soluble gas and argon as the insoluble gas. During a high concentration of nitrous oxide, argon increased from 3% to 10% concentration (second gas effect), indicating an overall volume loss. The loss of volume associated with the uptake of nitrous oxide concentrates the second gas (Miller, 2000), in this case argon.

Argon accumulation is a consequence of selective oxygen uptake. The two main determinants of this are the fresh gas flow rate from the oxygen concentrator and the rate of metabolic consumption of the subject (Friesen, 1992). In a semi-closed anesthesia circle system, oxygen is inhaled into the lungs, then exhaled into the breathing circuit, not the atmosphere. The exhaled gases pass through a carbon dioxide absorber that removes the carbon dioxide and some water vapor. The remaining gases are circled around to mix with the incoming fresh gas from the concentrator. Depending on the amount of gas in the circuit, gas is diverted back to the subject and/or to the environment. Over time, argon builds up in the breathing circuit and displaces oxygen. This causes the oxygen concentration being delivered to the subject to decrease, which may lead to hypoxia. To compensate for this problem, it has been proposed by Parker and Snowdon (1988) to either have a fresh gas flow rate at least 0.5 liter per minute or flush the circuit periodically. In this study, based on these findings, the fresh gas flow rates used were 0.5 liter per minute, 1 liter per minute, and 2 liters per minute.

#### Low Flow Anesthesia

Low flow anesthesia is a technique that is becoming more popular among anesthesia care providers, particularly in the military. When deployed during military conflicts, low flow anesthesia is used to conserve the oxygen resources available. Low flow anesthesia is a technique that uses low fresh gas flows of 0.5 liter per minute up to 3 liters per minute (Miller, 2000). Conventional anesthesia uses over 3 liters per minute. This supports the maximum flow rate of 2 liters per minute for this study as low flow anesthesia.

There are many advantages of low flow anesthesia compared to conventional anesthesia. Low fresh gas flows can lead to savings because less inhaled anesthetics will be required (Cotter, Petros, Dore,

Barber, & White, 1991). If there is less of a fresh gas flow, less gases are scavenged into the operating area producing less environmental pollution, thereby creating a safer environment for health care providers (Cotter et al., 1991). Low fresh gas flows improves inhalation gas humidity and decrease airway temperature loss over conventional anesthesia systems with higher fresh gas flows (Mizuno & Sumiyoshi, 1998). This is a benefit to field anesthesia where humidity moisture exchangers may not be available for use secondary to supply demands and logistical limitations.

Numerous studies have determined that anesthesia with low fresh gas flows is safe and used in many hospitals worldwide. The question is not whether to use low flow anesthesia, but rather how to use it safely (Grice, 1997). Experts have found that using low fresh gas flows is clinically safe and easily applicable (Igarashi, Watanabe, & Namiki, 1997; Okada et al., 1999). Okada et al. reported that the lowest fresh gas flow of 0.5 liters per minute, during low flow anesthesia, did not produce a low inspired oxygen concentration. Baum, Berghoff, Stanke, Petermeyer, and Kalff (1997) determined that desflurane could be used safely with low flow anesthesia. The Association for Low Flow Anesthesia (ALFA) was established to provide a forum to exchange ideas and to encourage research in all aspects of low flow anesthesia (Stevens, 1997).

#### Critique of Literature

In the literature, only two studies (Parker and Snowdon, 1988; Rathgeber et al., 1995) were found that have done similar research as this study. Parker and Snowdon (1988) reported on two experiments using the oxygen concentrator. The first experiment was on one healthy, nonsmoking volunteer, and the second experiment was on five anesthetized patients undergoing varicose vein surgery without cardiac, renal, or respiratory disease.

The first experiment by Parker and Snowdon (1988) used cylinders of gas comprising 90.5% oxygen and 9.5% argon. They used a semi-closed anesthesia circle system for flows of 0.5, 0.7, 0.9, and 2 liters per minute. At 0.31 liters per minute they used a closed anesthesia circle system. Their subject was conscious and spontaneously breathing through a mouthpiece. The 90.5% oxygen and 9.5% argon mixture used with this experiment was chosen to simulate the worst case clinical scenario with a properly functioning oxygen concentrator. They measured the argon fraction in end tidal gas, and found at each fresh gas flow rate the

argon fraction increased with time. Both the rate and extent of the increase in argon fraction were greater as the fresh gas flow rate was reduced. At the lowest flow rate (0.31 liter per minute), with the circle system closed, the end tidal argon fraction increased linearly about 0.3% per minute. The oxygen fraction decreased with time at a rate and to an extent related to the fresh gas flow. The nitrogen concentration increased through out the period of observation, it increased from 1% to 9% after 80 minutes at the lowest fresh gas flow rate. At higher flow rates, the increase in nitrogen fraction was much smaller and never exceeded 3% of the end tidal gas.

The second study used anesthetized surgical patients who were intubated and spontaneously ventilating. In this study they used the fresh gas mixture from the oxygen concentrator. They varied the amount of fresh gas flow and measured the oxygen concentration in the circuit. The argon concentration in the circuit increased as the fresh gas flow rate decreased while still maintaining a therapeutic oxygen concentration. At high fresh gas flow rates, some of the exhaled gas that would normally rejoin the inspired fresh gas overflowed and vented out of the circuit. At very low fresh gas flows, there was not enough exhaled gas to vent the accumulation of argon from the circuit. The increase in argon fraction was complimented by the decrease in the oxygen fraction at each fresh gas flow setting.

Parker and Snowdon (1988) found that at a fresh gas flow of 2 liters per minute, the argon concentration was approximately 10%. While a fresh gas flow of 0.5 liter per minute produced an argon concentration of approximately 20%, and a fresh gas flow of 0.31 liter per minute produced an argon concentration of approximately 40%. The argon concentration was measured until it stabilized or for a maximum of 90 minutes.

Parker and Snowdon (1988) stated that with the fresh gas flow of 0.31 liter per minute argon would continue to accumulate. At this very low fresh gas flow of 0.31 liter per minute, a 1 to 9% concentration of nitrogen was noted in the breathing circuit after 80 minutes. The authors did not discuss nitrogen concentration at any of the other flow rates, nor give a reason for the accumulation of this small percent of nitrogen.

Parker and Snowdon (1988) concluded that in a semi-closed anesthesia circuit, as long as fresh gas flows stayed above twice the patient's metabolic oxygen consumption and nitrous oxide was not used as a

part of the anesthetic, argon accumulation would not be an issue. If a fully closed anesthesia circuit is used, argon will accumulate until the circuit is opened. Therefore with low flow anesthesia, periodic flushing of the system is required to correct the problem of argon accumulation when using an oxygen concentrator.

Rathgeber et al. (1995) had results that were very similar to Parker and Snowdon despite their different study designs. Rathgeber et al. used a carbon dioxide producing, oxygen consuming metabolic lung to simulate a human lung instead of using human subjects. They concluded that the argon accumulation is flow-rate dependent. Argon did accumulate in rebreathing circuits, but only exceeded values higher than 10% at minimal flows of 0.5 liter per minute. Rathgeber et al. also concluded that using oxygen concentrators for anesthesia is safe and without risk of hypoxia, even in rebreathing systems.

Although both studies had similar recommendations, further research needs to be done. Argon accumulation in a semi-closed anesthesia circle system while using an oxygen concentrator has only been tested with a very small number of subjects and with an unspecified amount of experiments done using the metabolic lung.

The research done by Parker and Snowdon (1988) was very important in determining the variables for this study. This study uses the concept of argon accumulation, but modifies Parker and Snowdon's procedure to use the actual oxygen concentrator on healthy non-anesthetized subjects. The subjects in this study breathed through a semi-closed anesthesia circle system using a mouthpiece at three different fresh gas flows of 0.5, 1, and 2 liters per minute. The three different flow rates were evaluated to determine whether or not they were applicable and safe for anesthesia practice using the oxygen concentrator.

Many of the articles on argon in the literature described experimental studies using this inert gas. However, none described argon accumulation with the use of the oxygen concentrators. The articles referenced were selected to support the abundance of argon use in research. In 1979, there was an increase in the amount of research done on argon and other inert gases, and research began on the molecular sieve oxygen generating systems. Ikels and Adams (1979) compiled past research on argon, then made recommendations for future research involving argon, molecular sieve oxygen generating technology, and implications for military aviators.

Research using an experimental design with human subjects appears most in the literature. For example, Johnson et al. (1979) used five human subjects to measure inert gas absorption using nitrogen and argon. Horrigan et al. (1979) used eight human subjects breathing 80% argon and 20% oxygen to show that argon wash-in mirrors nitrogen wash-out. Hedenstierna and Santesson (1979) used nine human subjects when comparing argon and nitrogen to determine airway closure in anesthetized patients. Despite the amount of literature available discussing argon, the sample size of each of the studies is small. More recent research articles seem to be evenly divided using human subjects or lung models. Saidel and Lin (1986) used human subjects to determine if using argon as a non-invasive measurement tool could identify early lung abnormalities. Williams et al. (1994) conducted one of the experiments using a lung model instead of human subjects. Argon used in this instance measured dead space with an oscillating inspired signal. Winter (1995) did an experiment with an unidentified number of human subjects. His experiment showed clinical applicability on how an inert gas could be used as a non-invasive measure of effective pulmonary capillary blood flow.

#### Summary

The use of oxygen concentrators for home health is well-documented and common place in the United States and the United Kingdom. There are many anecdotal reports of the use of oxygen concentrators in non-rebreathing systems in underdeveloped countries. Oxygen concentrators are used because of their advantages of cost, convenience, and safety. However, there are few articles that describe using a circle system with the rebreathing of gases while using an oxygen concentrator. Oxygen concentrators can only use low flow rates in order to produce an oxygen product that is acceptable for use in anesthesia. Therefore, low flow anesthesia is a technique that must be employed.

As described in the literature, however, one of the dangers encountered with low flow anesthesia using this kind of system is that argon accumulates in the breathing circuit and displaces oxygen. The two major studies (Parker and Snowdon, 1988; Rathgeber et al., 1995) described how argon accumulates in a semi-closed anesthesia circle system when gas is delivered from the oxygen concentrator at low flow rates. There was also reference to the potential accumulation of nitrogen. This study design differs from these studies in that we used healthy non-anesthetized subjects using a semi-closed anesthesia circle system with

three different flow rates of 0.5 liter per minute, 1 liter per minute, and 2 liters per minute delivered by the oxygen concentrator.

## CHAPTER III

### Methodology

The purpose of this study was to determine the rate of oxygen dilution, resulting from argon accumulation, using three different fresh gas flow rates delivered by an oxygen concentrator in a semi-closed anesthesia circle system. The investigators used a non-experimental descriptive design.

Determination of oxygen dilution by argon accumulation was recorded for one group of unanesthetized subjects, each subject participated in three trials with flow rates of 0.5 liter per minute, 1 liter per minute, and 2 liters per minute. This chapter details the population, sample, and setting; instrumentation and procedure for data collection; protection of human subjects; the study design; and the procedure for data analysis.

#### Population, Sample, and Setting

This population was a convenience sample of nine subjects from healthy volunteers in a graduate nurse anesthesia program that included both students and faculty. The graduate nurse anesthesia program is located at a military academy in the south central United States. The study was conducted in the Graduate Nurse Anesthesia Classroom/Lab.

The subjects selected were eighteen years of age or older, legally competent to give informed consent, and capable of understanding the English language. All subjects were in good health, and free from any chronic or acute disease or illness. Subjects were excluded if there was a history of: (a) acute or chronic disease or illness involving the cardiac or respiratory systems in the past six months; (b) pregnancy or breast feeding; (c) smoking in the past year; (d) upper respiratory infections within the past month, including the common cold or flu; (e) use of prescriptive or over the counter medications for treatment of disease or illness; or (f) history of claustrophobia. Additional exclusion criteria include: (a) systolic blood pressure greater than 140 or less than 90; (b) diastolic blood pressure greater than 90 or less than 50; (c) heart rate greater than 100 or less than 50; and (d) temperature greater than 99 degrees Fahrenheit. Subjects meeting the exclusion criteria were not allowed to participate in this study. This was a study on healthy subjects, therefore there was no alternative treatment.

### Sample size

A power analysis was performed to determine a sample size that would provide enough data to produce strong, credible results. The research of Parker and Snowdon (1988) suggests that in the anesthetized patients the standard deviation in oxygen concentration across subjects was 1%. It is estimated that it will be as high as 2 % in unanesthetized subjects. Parker and Snowdon (1988) found a 5% difference in argon accumulation across different flow rates, a very large effect size. It was estimated that the difference in this study would be somewhat smaller, approximately 4%, due to the difference in the procedure, the difference in equipment, and the difference in the experience of the researchers. Thus, a sample of nine subjects provided a power  $\geq 0.80$ , when alpha was set at 0.01, the effect size was estimated to be a mean difference between flow rates of 2.0 standard deviations, and a one-way repeated measures analysis of variance (ANOVA) was used to analyze oxygen concentration. The repeated measures design used in this study was very powerful and therefore a relatively small number of subjects were required. An alpha smaller than the conventionally used was chosen to insure that the results of the study would be highly credible, despite the small number of subjects used.

### Subjects

The investigators used a convenience sample of volunteers. Subjects were recruited for the study from the graduate nurse anesthesia program student and faculty population. Potential participants were briefed on the study and criteria for selection in a classroom environment, and a volunteer sign-up list was circulated at the end of the briefing. Volunteers were contacted, within two days, by the investigators for individual counseling appointments. If there had not have been enough volunteers, other groups would have been asked to participate until the sample size was reached. Other graduate students would have been asked to volunteer. Enlisted students were not asked to participate; they were excluded to prevent a misperception of coercion. Data collection continued until the sample size of nine was obtained for statistical analysis. Subjects each completed three trials using different gas flow rates of the following: 0.5 liter per minute, 1 liter per minute, and 2 liters per minute from the oxygen concentrator. The order of the flow rates were counterbalanced to insure that every flow rate appeared an equal number of times in each order position. Counterbalancing insured that there were no order effects of testing.

### Instrumentation

All equipment was provided by the Anesthesia Department of a military hospital and from the military academy in the south central United States. All equipment was calibrated for accuracy and precision by appropriately trained personnel prior to the start of the study according to manufacturer's specifications. The oxygen concentrator, gas analyzer, and pulse oximeter were checked for accuracy and re-calibrated prior to the start of each trial based on manufacturer's recommendations. Routine maintenance was done according to the manufacturer's recommendations. Routine cleaning was done by the investigators based on manufacturer's recommendations. Problems with the equipment's function or accuracy were directed to the medical maintenance department or the manufacturer, if there were any.

#### Cole Parmer Flow Meter.

This flow meter had been engineered to be precise and accurate at gas flows of 5 liters per minute or less, with less than 0.05 liter per minute error. The flow meter was calibrated on March 28, 2000. Litton Life Support provided a precision and accuracy flow diagram for this specific flow meter. It uses a numeric scale of 0-150 based on the desired flow rate. The letter and calibration graph from the engineers is included in Appendix A.

The oxygen flow meter on the oxygen concentrator was used to adjust the gas flow to the Cole Parmer flow meter. The actual gas flow to the subject was based on the specific numeric reading of the Cole Parmer flow meter that was downstream from the oxygen concentrator.

#### Ohmeda Rascal® II, Anesthetic Gas Monitor.

The Ohmeda Rascal® II, Anesthetic Gas Monitor used a patented Laser-Raman™ light scattering technology that performed inspired and expired gas analysis for anesthesia. This monitor is commonly used in the operating room environment. Gases detected by this monitor include oxygen, carbon dioxide, nitrogen, nitrous oxide, and volatile anesthetic agents. According to manufacturer's specifications, the range and accuracy (three standard deviation confidence limits) for these gases were as follows. Oxygen had a range of 0-100% volume, and an accuracy of  $\pm 2$  volume % (below 40 volume %). Carbon dioxide had a range of 0-10 volume % and 0-100mmHg, and an accuracy of  $\pm 3$ mmHg. Nitrogen had a range of 0-100 volume %, and an accuracy of  $\pm 4$  volume %. Volatile agents and nitrous oxide were not used in this

study. There was a recommended 15 minute warm up time to meet specifications. Auto calibration occurred when the monitor was turned on, and took 30 seconds. Time response to carbon dioxide and oxygen was less than or equal to 350 milliseconds. Displays of gas concentrations, waveforms, and trends were available. The water separator assembly removed most water. Water vapor that passed through the assembly was mostly equilibrated with room air humidity by special Nafion™ tubing, the remaining water vapor that passed through the monitor detector was ignored. This monitor was calibrated according to manufacturer's recommendation before the start of the study and every thirty days by a certified nurse anesthetist that was a member of the faculty. Automatic calibration was done daily according to manufacturer's recommendations. Any problems identified were addressed to the faculty advisor, biomedical maintenance, or to the manufacturer as needed. No problems were encountered.

#### Ohmeda Oxygen Analyzer (5120).

A second oxygen gas analyzer monitored the oxygen concentration delivered to the circle system from either the prefilled oxygen cylinder or from the oxygen concentrator. This monitor was placed in line prior to the circle system to monitor oxygen concentration that was delivered to the inspiratory circuit of the semi-closed anesthesia circle system. The oxygen sensor was calibrated to room air daily. The investigators were trained to do this under the direction of a certified registered nurse anesthetist that was a faculty member. Any problems identified were checked by the certified registered nurse anesthetist.

#### Total O<sub>2</sub> Delivery System Oxygen Concentrator.

The oxygen concentrator, Chad Therapeutics model # TO-001 (HC-311-00) used a pressure swing absorption technology. Direct performance of gas flow was 0-3 liters per minute. By specifications, the oxygen production was  $93\% \pm 3\%$ , and cylinder fill pressure was 2000 psig. The oxygen concentrator was designed with a oxygen purity sensor indicator which illuminated a green light that oxygen was being generated at 90% or better purity, a yellow light signified lower purity but still adequate oxygen concentration, and a red light indicated system failure (<85%). The Total O<sub>2</sub> Delivery System was able to produce oxygen that was delivered to the circuit up to 3 liters per minute, and filled an oxygen cylinder at 0.5 liter per minute. The oxygen cylinders used in this study contained the oxygen gas mixture produced by the oxygen concentrator.

#### Oxygen Concentrator's Tank Flow Meter.

There were two oxygen cylinders with modified pressure reducers that were to be used with the oxygen concentrator. Testing for precision and accuracy was done at Litton Life Support. In a letter (Appendix B) accompanying the oxygen cylinders, the engineer wrote that the flow rates on the pressure reducers were above 10 liters per minute when the cylinder pressure was above 300 psi. The maximum flow rate was 12 liters at 2000 psi. The engineer supplied graphs specific to each cylinder confirming those rates. Those cylinder tanks insured a 10 liter flow rate to denitrogenate and preoxygenate the subject.

#### Demographic Data and Health History Tool.

A 30 item tool (Appendix C) was developed by the investigators to screen subjects for a pertinent health history, exclusion criteria, and basic demographic data. The tool was used to gather health history for inclusion and exclusion criteria. Demographic data was collected to describe the sample in the study.

#### Procedure for Data Collection

Subjects were volunteers from the student and faculty population of a nurse anesthesia program in the south central United States. Potential participants were briefed on the study and criteria for selection in a classroom environment, and a volunteer sign-up list was circulated at the end of the briefing. Within two days, volunteers were contacted by the investigators for individual counseling appointments. A private conference area was used for each individual counseling session. The subject was given a chance to read the consent thoroughly, ask questions, and be given a copy of the informed consent if requested (Appendix D). All questions were answered to the subject's satisfaction. The informed consent and health history were then obtained. Privacy was maintained at all times. A brief note was written in the subject's medical record stating the name of the study, number of trials, and how to contact the principal investigator.

#### Protocol

Each subject underwent three trials using different oxygen flow rates, 0.5 liter per minute, 1 liter per minute, and 2 liters per minute from the oxygen concentrator. The order of the flow rates were counter-balanced to insure that every flow rate appeared an equal number of times in each order position. Counter-balancing insured that there were no order effects of testing. Each trial consisted of the subject breathing through a semi-closed anesthesia circle system, while using a mouth piece and nose clip, at one of the

designated flow rates. The trial continued until there was 1% or less change in the oxygen concentration in the expired gas concentration over any 10 minute period indicating a plateau had been reached, with a minimum of 30 minutes. If a plateau was not identified, the trial ended at 120 minutes. A semi-closed circuit was maintained through out each trial. A timer was used for recording purposes. All data were documented on the Data Collection Tool (Appendix E).

#### Procedure

1. Informed consent was obtained from the subject. The health history was completed or updated before each trial. Inclusion and exclusion criteria were reviewed.
2. Each subject was scheduled for three trials. The order of the trials were counterbalanced.
3. Prior to the study the equipment was calibrated per manufacturers' recommendations. The Ohmeda Rascal® II Gas Analyzer passed inspection by biomedical and calibrated every 30 days by a certified registered nurse anesthetist faculty member. The Ohmeda oxygen analyzer (5120) was calibrated daily by the investigators after training by a certified registered nurse anesthetist faculty member. The Total O<sub>2</sub> Delivery System passed inspection by the manufacturer prior to use, and filters were cleaned by the investigators according to manufacturer's recommendations. The Cole Parmer flow meter was checked for accuracy prior to use by the engineers.
4. Pretrial:
  - a) Auto-calibration of the Ohmeda Rascal® II Gas Analyzer occurred when the monitor was turned on. This was repeated at 1, 2, 2 ½, 5, 10, 20, and 40 minutes after the machine was turned on. Thereafter, auto-calibration was repeated every 81 minutes. Quality control checks using compressed gases from the manufacturer were performed at the start of the study then monthly thereafter, by a certified registered nurse anesthetist faculty member. Failure to pass these calibrations at any time would have resulted in stopping the trial and contacting medical maintenance or the manufacturer to service the equipment. The Ohmeda oxygen analyzer (5120) was calibrated daily to room air. The Total O<sub>2</sub> Delivery System Oxygen Concentrator was turned on, operation was according to manufacturer's recommendations and instructions. The oxygen purity sensor light was checked and verified to be illuminating

green. If the light was illuminating yellow or red, the manufacturer would be contacted.

The previously calibrated Cole Parmer flow meter was verified to be level prior to the start of each trial (a level was on the base of the flow meter for this purpose).

- b) For each trial, a single use breathing circuit and a fresh carbon dioxide absorbent canister placed inline in the expiratory limb was attached to the fresh gas tubing. Each circuit was visually and pressure checked for leaks.
  - c) At the start of the trial, a baseline oxygen concentration level was obtained from the oxygen cylinder and then 10 minutes later from the oxygen concentrator after preoxygenation and denitrogenation was accomplished. The oxygen cylinder or the oxygen concentrator brought the gas mixture to the inspiratory limb of the circuit. Baseline oxygen content from the oxygen cylinder, produced from the oxygen concentrator, and the oxygen concentrator itself was set to manufacturer's recommendation of  $93\% \pm 3\%$  oxygen, while the remaining gases were argon and nitrogen. If these levels were not obtained, the trial did not begin. These oxygen concentration levels were recorded every 5 minutes throughout the trial.
5. The subject was positioned comfortably in a sitting position. The health history was updated for any pertinent changes that may have occurred. If any of the exclusion criteria was met, the subject would have been re-evaluated for inclusion in the study. Comfort of the subject during each trial was maintained with environmental adjustments (positioning, room temperature, music, and lighting) as needed.
  6. Baseline vital signs, ECG, and pulse oximetry were obtained and evaluated. If baseline vital signs were any of the following: systolic blood pressure greater than 140 or less than 90; diastolic blood pressure greater than 90 or less than 50; heart rate greater than 100 or less than 50; temperature greater than 99 degrees Fahrenheit, a cardiac rhythm other than sinus rhythm, or a pulse oximetry reading less than 96%, the subject would have been excluded from the study. Baseline data was recorded on the data sheet.
  7. The subject was instructed to breathe through a semi-closed anesthesia circle system using a mouth piece and nose clip, at one of the designated flow rates. The subject received the oxygen

mixture from the oxygen cylinder at 10 liters per minute through the semi-closed anesthesia circle system for 10 minutes. This oxygen cylinder contained oxygen produced by the oxygen concentrator. This denitrogenation and preoxygenation removed the concentration of nitrogen from the circuit and subject's lungs.

8. Following denitrogenation, a predetermined flow rate was delivered to the subject, according to the trial. The oxygen concentrator's flow rate was adjusted to the numeric value determined by the Cole Parmer flow meter for precise flow. The subject always received gas produced from the oxygen concentrator. Gas analyzer concentrations for inspired and expired oxygen, carbon dioxide, and nitrogen were recorded every 5 minutes, and were visually monitored by one of the investigators through out the trial.
9. Ohmeda Rascal II ® gas analyzers obtained constant readings of the oxygen, carbon dioxide, and nitrogen content in the inspiratory and expiratory gases in the semi-closed anesthesia circle system. In addition, the Ohmeda oxygen analyzer analyzed oxygen gas content delivered to the inspired limb of the semi-closed anesthesia circle system from the oxygen concentrator and oxygen tank. An inspired oxygen concentration  $\geq 21\%$  was returned to the expiratory limb of the circuit prior to the carbon dioxide absorber.
10. Most, if not all, exhaled gases flowed through the carbon dioxide absorbent canister. If there was a measurement of carbon dioxide ( $\geq 2\%$ ) in the inspiratory limb, the trial would have been terminated. If the carbon dioxide granules changed to a purple color, this indicated that the absorber was exhausted and the trial would have been stopped.
11. The APL valve in the expiratory limb was adjusted, as needed, to release any excess gas within the circuit for each flow rate. The APL valve maintained a constant volume in the semi-closed anesthesia circle system. System volume was constant when the reservoir bag returned to the same volume with each breath. Slight positive pressure created an outward venting which was expected. In the event of negative pressure, the reservoir bag would collapse, and air would be entrained into the circuit. This high sudden influx of nitrogen would terminate the trial, although this did not occur in this study.

12. The subject had continuous monitoring of electrocardiogram, pulse oximetry, and numeric and waveform end-tidal carbon dioxide. Routine recording of heart rate, respiratory rate, and non-invasive blood pressure was recorded at baseline, every 10 minutes during the trial, and at the conclusion of each trial. Skin temperature was taken at baseline and at the conclusion of the trial. If at any time the subject deviated from their normal baseline range for heart rate or blood pressure by 20%, have any abnormalities observed from the ECG, have abnormal end-tidal carbon dioxide accumulation, have  $\geq 2\%$  inspired carbon dioxide content, or an oxygen saturation less than 96%, the trial would have been terminated.
13. The trial would have been terminated if the subject complained of any untoward symptoms or requested to stop. The investigators collected all data and monitored the subjects throughout the trial for any problems. The subject remained awake for each trial.
14. One hundred percent oxygen was available if needed. If the subject, under any circumstances required immediate medical care beyond the capabilities of the investigators and the certified registered nurse anesthetist faculty member, emergency medical services were to be called.

#### Interrater Reliability

All three investigators received training on reading and interpretation of the Ohmeda Rascal II ® gas analyzer from a certified registered nurse anesthetist until 100% interrater reliability was achieved. At least two investigators were present for each trial. Each investigator had a specific duty assigned during the trial. The investigators recorded digitally displayed inspired and expired gas analysis data every 5 minutes, vital signs and oxygen saturation every 10 minutes, and the oxygen concentration from the oxygen source every 5 minutes. Both investigators continually monitored all aspects of the trial and maintained the subject's comfort.

#### Protection of Human Subjects

Informed consent was obtained from each subject after a thorough briefing describing the study, inclusion and exclusion criteria, and risks and benefits as outlined in the informed consent (Appendix D). All questions were answered. A copy of the informed consent was offered and given to the subject if requested. The investigators kept the subject informed of any changes that arose, and notified the subject if

any untoward effects were determined. Results of this study will be disseminated in accordance with the University of Texas Health Science Center at Houston and the United States Army requirements.

Confidentiality was maintained at all times. The subjects were assigned a number and identified by that number only on all data records. Only the principal investigator had the original name list and the assigned numbers, and secured this in a separate location. Data was secured in a locked box in the anesthesia classroom. Data will be released as aggregate data. Anonymity in any publication resulting from this study will be maintained. All records will be kept in a secure location by the principal investigator for five years after completion of the study.

There were no alternative treatments because the study did not involve treatments. There was no known benefit to the subject, other than maybe the contribution to the body of research. In the case of anesthesia students, they experienced breathing within a circle system that is commonly used in anesthesia practice and therefore might help them be sensitive to patient's feelings in the future.

Careful screening and monitoring of subjects was to minimize any potential risks. Previous research has used pre-filled cylinders of a specific oxygen/argon mixture producing known oxygen and argon levels (Parker & Snowden, 1988). Whereas, this study used gas flow directly from the oxygen concentrator, which produced various oxygen and argon levels. Oxygen concentrators are currently being used by Forward Surgical Teams with the draw-over anesthesia system. The subject experienced slight pressure from the nose clip and their lips got tired from holding the mouthpiece. The subjects experienced slight pressure from the pulse oximeter clip on the finger, some pressure from the inflation of the blood pressure cuff, and the sticky ECG pads pulled the skin and hair on removal. Any risk of delivering a hypoxic gas mixture to the subject was extremely slight. The gas mixture was analyzed through out the trial and there was constant vigilance of the subject. The trial was terminated if the subject complained of untoward symptoms. A senior faculty member was available during the trials. Emergency medical services were to be activated if needed.

#### Study Design

This study was a prospective, non-experimental, descriptive design. From the power analysis, it was determined to have one group of nine subjects with three trials for a total of 27 intervals. Subjects were a

convenience sample of students and faculty from a graduate nurse anesthesia program at a military academy in the south central United States. A one group design allowed a better control of physiological variables by using the same subjects for each trial. This allowed a better comparison of parameters between flow rates used. Although the intervention was altered to the subject by varying the flow rate, there was no control group to make this an experimental design. This non-experimental, descriptive design was best to observe, describe, and document the relationship between inspired oxygen concentration and gas flow rate from the oxygen concentrator. By tightly controlling the gas flow and monitoring the concentration of inspired and expired gases, trends of oxygen dilution with the various gas flows used were evident.

#### Procedure for Data Analysis

For data analysis, a one-way repeated measures analysis of variance was used to analyze oxygen concentration. This choice was based on the need to compare three trials of ratio level data on oxygen concentration, for one sample of subjects. The null hypothesis stated that we will see no statistically significant difference in the data we collect for each trial as we changed our flow rates. The mean and standard deviation of demographic data was reported to better describe the subject population.

## CHAPTER IV

### Analysis of the Data

In this chapter, the investigators discuss data and data analysis for this study. Specifically, sample characteristics, primary findings, and secondary findings are discussed. Data analysis was performed using SPSS® version 10.0 for Windows.

#### Sample Characteristics

##### Sample

The convenience sample in this study was drawn from healthy volunteers in a graduate nurse anesthesia program that included both students and faculty at a military academy in the south central United States. Eighteen volunteers signed up to participate in the study. There was no attrition before or during the study. The first nine volunteers on the list met the inclusion criteria, participated, and completed the study.

Sample characteristics for the nine subjects, four females and five males, who were enrolled in the study are shown in Table 1. Demographics included age, gender, height, weight, and body mass index (BMI). These demographics were chosen to describe the physical size of the subjects. The sample characteristics reflected the average adult height and weight similar to the general population (Miller, 2000), so the assumption of normal lung size (volumes and capacities) for this subject group was made. All the volunteers were Caucasian due to the available volunteers and small sample size. Sample characteristics were obtained during the health history interview from each subject (Appendix C). The mean age, which was obtained in actual total years only, was 32.56 years ( $SD=6.11$ ) with a range of 26 to 41 years of age. More males (three) were in the younger age group of 26-29 than females (one). One male was in the age group 30-35. More females (three) were in the older age group of 36-41 than males (one). The mean height was 176.06 centimeters ( $SD=8.71$ ) with a range of 165.1 to 187.9 centimeters. The mean height for male subjects was 182.3 centimeters (range of 172.7 to 187.9 centimeters), and for female subjects was 168.2 centimeters (range of 165.1 to 172.7 centimeters). The mean weight was 77.82 kilograms ( $SD=12.12$ ) with a range from 63.63 to 100 kilograms. The mean weight for males was 84.8 kilograms (range of 76.38 to 100 kilograms) and for females 69 kilograms (range of 63.63 to 80.45 kilograms). The mean BMI was

Table 1

Subject Characteristics

Characteristic	n (%)	Male (%) [n = 5]	Female (%) [n = 4]
Age			
26-29	4 (44.45)	3 (75)	1 (25)
30-35	1 (11.1)	1 (100)	0 (0)
36-41	4 (44.45)	1 (25)	3 (75)
Height			
165-171	3 (33.33)	0 (0)	3 (100)
172-180	2 (22.22)	1 (50)	1 (50)
181-188	4 (44.45)	4 (100)	0 (0)
Weight			
63-75	3 (33.33)	0 (0)	3 (100)
76-85	4 (44.45)	3 (75)	1 (25)
86-100	2 (22.22)	2 (100)	0 (0)
BMI			
22-24	5 (55.6)	2 (40)	3 (60)
25-27	3 (33.3)	2 (66.7)	1 (33.3)
28-30	1 (11.1)	1 (100)	0 (0)

Note. Percent for n = percent of total subject population. Others are for the percent of the n for that characteristic. Age = Years, Height = Centimeters, Weight = Kilograms, BMI = Body Mass Index.

24.99 ( $SD=2.39$ ) with a range from 22.64 to 29.90. The mean BMI for males was 25.49 (range of 22.83 to 29.90). The mean BMI for females was 24.35 (range of 22.64 to 26.97).

#### Data Collection Points

Each subject participated in three trials, and all trials had the same data collection points for the first 30 minutes. Although a plateau was defined for termination of a trial, a minimum trial time of 30 minutes was set based on a previous research study (Parker & Snowdon, 1988). A digital timer was used as the clock, and data was collected at 0, 5, 10, 15, 20, 25, and 30 minutes. This pattern continued if a plateau was not reached to a maximum of 120 minutes. To insure the health of each subject, each trial consisted of a baseline assessment and recording of physical parameters. Continuous monitoring and recording of blood pressure, heart rate and rhythm, respiratory rate, temperature, and oxygen saturation were done every ten minutes to monitor the subject's physiologic response (i.e. 0, 10, 20, 30 minutes). In addition, the primary dependent variables of the inspired and expired concentrations of oxygen, carbon dioxide, nitrogen, and argon were recorded at baseline and at each 5 minute intervals (i.e. 0, 5, 10, 15, 20, 25, 30 minutes). Therefore, the data collection points used for the gas analysis were baseline, 15 minutes, and 30 minutes. Since, all subjects in all trials had the same data collection points for the first 30 minutes; these three data collection points (baseline, 15 minutes, and 30 minutes) were used to analyze the trend in the inspired gas concentrations. If a plateau in the expired oxygen concentration was reached at 30 minutes, the trial was stopped. Otherwise, data collection continued until a plateau was reached or a maximum of 120 minutes. The time intervals for the data collection points remained the same throughout each trial until termination.

#### Baseline Assessment.

The subject's baseline blood pressure, heart rate and rhythm, respiratory rate, temperature, and oxygen saturation were measured at the start of each trial. Baseline values and subsequent data were recorded on the Data Collection Tool (Appendix E). These baseline values were compared to the established exclusion criteria values in the protocol. At baseline, none of the subjects were excluded. In accordance with the exclusion criteria, the subjects did not smoke; have respiratory, cardiac, or other chronic diseases that would influence their pulmonary status; have any possibility of pregnancy; or have a recent cold or flu. Therefore, all the subjects were considered healthy adults to participate in this study.

Subsequent monitoring and recording of this assessment data were done every 10 minutes. Per protocol, a 20% range from the baseline value was established for blood pressure, heart rate, and respiratory rate for comparison during the trial. If the subject deviated greater than 20% above or below their baseline value, the trial would have been stopped. All subjects stayed within 20% of their baseline values; therefore, none of the trials had to be terminated for this reason. During all trials, all subjects remained above a 98% oxygen saturation.

#### Gas Analysis.

The oxygen concentration delivered to the subject, directly from either the oxygen concentrator or from the oxygen tank (that was filled by the oxygen concentrator), was measured at the start of the study and at 5 minute intervals. The inspired and expired gas concentrations of oxygen, carbon dioxide, nitrogen, and argon levels from the subject were recorded at the beginning of the trial, and at 5 minute intervals. These concentrations were recorded on the Data Collection Tool (Appendix E).

The actual number of data collection points varied for each subject because the length of each trial ranged from a minimum of 30 minutes to a maximum of 120 minutes (Table 2). All subjects had the same data collection points up to 30 minutes. The trial was stopped when a plateau was reached at 30 minutes, or the trial continued until a plateau was reached or a maximum of 120 minutes. A plateau was defined in the protocol as a 1% or less change in the expired oxygen concentration over any 10 minute interval (three consecutive recordings). All but 3 of the 27 trials terminated when a plateau was reached. All but one of the 2 liter flow rate trials were completed by 50 minutes, one subject completed the trial at 70 minutes. All of the 1 liter flow rate trials were completed by 65 minutes. During the 0.5 liter flow rate, all subjects completed the data collection points up to 75 minutes. Three trials, which were all during the 0.5 liter flow rate, reached the maximum time of 120 minutes, which terminated the trial. Only one subject complained of a headache upon completion of one of the trials (0.5 liter per minute).

In summary, the data collection points were at 0, 5, 10, 15, 20, 25, and 30 minutes for all trials, this pattern continued if a plateau was not reached. Specifically, the inspired oxygen concentration of the fresh gas from the oxygen concentrator, and the inspired and expired gas concentrations of oxygen, carbon dioxide, and nitrogen were measured directly every 5 minutes. Argon was measured indirectly at the

Table 2

Total Subjects at Each Data Collection Point

Time* (minutes)	2 Liters	1 Liter	0.5 Liter
30	9	9	9
35	4	4	9
40	2	3	9
45	2	3	9
50	2	3	9
55	1	3	9
60	1	3	9
65	1	2	9
70	1	0	9
75	0	0	9
80	0	0	7
85	0	0	6
90	0	0	5
95	0	0	4
100	0	0	4
105	0	0	4
110	0	0	4
115	0	0	3
120	0	0	3

Note. \*The minimum length of a trial was 30 minutes.

same 5 minute intervals. Each trial had data collection points every 10 minutes for physiological parameters of blood pressure, heart rate, respiratory rate, and oxygen saturation to monitor the physical well being of the subject. Therefore, after baseline, the data collection points for gas concentration (dependent variable) were on the 5 minute intervals, and assessment data (physiological health monitoring) was also collected on the same 10 minute intervals until the trial was terminated. Subjects were assigned to the flow rate (independent variable) for each trial (0.5 liter per minute, 1 liter per minute, 2 liters per minute) based on the original counterbalancing of the order of each trial. The subject collaborated with the investigators on the schedule of the assigned three trials and the time interval between each trial.

#### Primary Findings

This study was designed to determine the rate of oxygen dilution, resulting from argon accumulation, using three different low fresh gas flow rates while using an oxygen concentrator in a semi-closed anesthesia circle system.

Hypothesis: There will be an increase in the rate of oxygen dilution, while remaining above an inspired oxygen concentration of 21%, by argon, as flow rates decrease in a semi-closed anesthesia circle system using an oxygen concentrator for the fresh gas source.

A power analysis was calculated to determine a sample size that would produce strong, credible results. The standard deviation across unanesthetized subjects for oxygen concentration was estimated to be 2%, and the difference in argon accumulation across flow rates (0.5 liter per minute, 1 liter per minute, and 2 liters per minute) would be 4%. This estimation was based on the results of a similar study (Parker & Snowdon, 1988). Thus, a sample of nine subjects would provide a power  $\geq 0.80$ , when alpha is set at 0.01; the effect size was estimated to be a mean difference between flow rates of 2.0 standard deviations. An alpha of 0.01 was used to establish statistical significance. Medical and nursing research commonly uses an alpha of 0.05 for establishing significance of the results. An alpha smaller than 0.05 was used to insure credible study results despite the small number of subjects. A one-way repeated measures ANOVA was used to analyze the differences of the inspired oxygen concentration. This statistical test was used to test the difference among the means of the three related groups.

The three fresh gas flow rates (0.5 liter per minute, 1 liter per minute, and 2 liters per minute) were analyzed for inspired oxygen concentration at baseline, at 15 minutes, and at 30 minutes for each subject. As the flow rate decreased, the inspired oxygen concentration also decreased over time. In contrast, the argon and nitrogen concentrations increased. As shown in Table 3, the baseline inspired oxygen was a mean of 96.22% at 2 liters per minute, 96.88% at 1 liter per minute, and 96.44% at 0.5 liter per minute. The difference across flow rates in the inspired oxygen concentration is seen at the 15 and 30 minute intervals. There is an increase in the rate of oxygen dilution as flow rates decrease in a semi-closed anesthesia circle system. The inspired oxygen concentration at 15 minutes was a mean of 90.11% ( $SD=5.77$ ) at 2 liters per minute, 87.33% ( $SD=2.83$ ) at 1 liter per minute, and 82.22% ( $SD=2.43$ ) at 0.5 liter per minute. The inspired oxygen concentration at 30 minutes was a mean of 91.22% ( $SD=4.73$ ) at 2 liters per minute, 86.11% ( $SD=5.46$ ) at 1 liter per minute, and 74.44% ( $SD=3.57$ ) at 0.5 liter per minute. There was a small decrease in the inspired oxygen concentration between the flow rates of 2 liters per minute and 1 liter per minute at the 15 and 30 minute intervals (Table 3). There was a larger decrease in the inspired oxygen concentration between the 1 liter per minute and the 0.5 liter per minute flow rate, and between the 2 liters per minute and the 0.5 liter per minute flow rate at the 15 and 30 minute intervals.

A one-way repeated measures ANOVA used for this study, uses a within-subjects test. A repeated measures design uses a single group of subjects, this allows subjects to serve as their own controls. A one-way repeated measures ANOVA is the statistical test used to test the difference among the means of these three related groups. The  $F$  statistic is the correct parametric test to be used with the repeated measures ANOVA. The computation of the  $F$  statistic is the sum of the squared deviations around the mean. The sum of squares within-subjects captures the variation of each individual relative to the mean of the group (Polit, 1996). The mean amount of variation is determined by dividing the sum of the squared deviations by degrees of freedom (df). Degrees of freedom indicate the number of components that are free to vary about the mean. The corrected  $F$  test takes into account sampling error and effect of the independent variable. An  $F$  value of 1.0 is expected if the null hypothesis was true. The  $F$  test was followed with multiple pairwise comparisons that were corrected by a Bonferroni adjustment. A Bonferroni adjustment increases the critical value so that it is harder to find a critical difference, and insures that the differences found are actual.

Table 3

Mean Inspired Concentration of Oxygen and Argon at Baseline, 15 Minutes, and 30 Minutes

	Baseline		15 minutes		30 minutes	
Flow Rate	<u>M</u>	<u>SD</u>	<u>M</u>	<u>SD</u>	<u>M</u>	<u>SD</u>
2 L/min						
Oxygen	96.22	0.97	90.11	5.77	91.22	4.73
Argon	2.85	0.68	3.77	0.79	4.04	0.89
1 L/min						
Oxygen	96.88	1.05	87.33	2.83	86.11	5.46
Argon	2.72	0.98	5.08	1.07	5.26	1.14
0.5 L/min						
Oxygen	96.44	1.74	82.22	2.43	74.44	3.57
Argon	2.92	1.30	6.69	0.82	8.70	1.16

Note. All above values are in percent.

A statistically significant difference across flow rates was seen for inspired oxygen concentration,  $F(2,16) = 23.05$ ,  $p < 0.0001$ ,  $\beta = 1.000$  (Table 4). A statistically significant difference across time was also seen,  $F(2,16) = 106.34$ ,  $p < 0.0001$ ,  $\beta = 1.000$ . Based on the computed values and analysis for this study, in which a statistically significant difference for inspired oxygen concentration was observed, the hypothesis was accepted.

Table 4

Test of Within-Subjects Effects for Oxygen and Argon

Gas	Actual $F$ Value (Flow Rate)	Actual $F$ Value (Time)	Significance	Observed Power (Flow Rate/Time)
Oxygen	23.05	106.34	<.0001	1.000/1.000
Argon	21.71	119.67	<.0001	1.000/1.000

Note. Critical value of  $F=6.23$  (2,16 df);  $\alpha=0.01$ .

A statistically significant difference across flow rates in argon accumulation was seen,  $F(2,16) = 21.71$ ,  $p < 0.0001$ ,  $\beta = 1.000$ . A statistically significant difference across time for argon accumulation was also seen,  $F(2,16) = 119.67$ ,  $p < 0.0001$ ,  $\beta = 1.000$ . As the inspired argon concentration increased across flow rates, there was a concurrent decrease in the inspired oxygen concentration. Therefore, significant differences in both oxygen dilution and argon accumulation were seen.

Using pairwise comparisons (Table 5) of the three different flow rates of inspired oxygen concentration, there is a statistically significant difference between the 0.5 liter per minute ( $M=84.37$ ,  $SE=0.72$ ) and 1 liter ( $M=90.11$ ,  $SE=0.96$ ) per minute flow rates ( $M$  difference =  $\pm 5.741$ ,  $SE=1.311$ ,  $p=0.007$ ), and between 0.5 liter per minute ( $M=84.37$ ,  $SE=0.72$ ) and 2 liters per minute ( $M=92.52$ ,  $SE=1.25$ ) flow rates ( $M$  difference =  $\pm 8.148$ ,  $SE=1.451$ ,  $p=0.002$ ). Statistical significance was not found between 1 liter per minute ( $M=90.11$ ,  $SE=0.96$ ) and 2 liters per minute ( $M=92.52$ ,  $SE=1.25$ ) flow rates ( $M$  difference =  $\pm 2.407$ ,  $SE=0.858$ ,  $p=0.069$ ).

Table 5

Pairwise Comparisons of Three Different Flow Rates for Oxygen & Argon

Flow rate comparison	Gas	Mean difference	Standard error	Significance
0.5 L/min:1 L/min <sup>†</sup>				
	Oxygen	±5.741	1.311	.007*
	Argon	±1.748	.536	.034
0.5 L/min:2 L/min <sup>†</sup>				
	Oxygen	±8.148	1.451	.002*
	Argon	±2.544	.314	.000*
1 L/min:2 L/min <sup>†</sup>				
	Oxygen	±2.407	.858	.069
	Argon	±0.796	.288	.073

Note. \* Statistically significant at the 0.01 level. <sup>†</sup> Flow rate comparison was done in both directions.

Using pairwise comparisons of the three different flow rates for inspired argon concentration, there is a statistically significant difference between 0.5 liter per minute ( $\underline{M}=6.10$ ,  $\underline{SE}=0.33$ ) and 2 liters per minute ( $\underline{M}=3.56$ ,  $\underline{SE}=0.22$ ) flow rates ( $\underline{M}$  difference =  $\pm 2.544$ ,  $\underline{SE} = 0.314$ ,  $p < 0.0001$ ). There is a difference between 0.5 liter per minute ( $\underline{M}=6.10$ ,  $\underline{SE}=0.33$ ) and 1 liter per minute ( $\underline{M}=4.36$ ,  $\underline{SE}=0.33$ ) flow rates ( $\underline{M}$  difference =  $\pm 1.748$ ,  $\underline{SE} = 0.536$ ,  $p = 0.034$ ). Although this difference is not considered statistically significant at an alpha of 0.01, medical and nursing literature accept an alpha of 0.05 as statistically significant. The investigators recognize that using a Bonferroni adjustment during pairwise comparisons creates a larger critical value to exceed for significance. Therefore, the investigators recognize that obtaining a  $p = 0.034$  still is a clinically significant difference even with an alpha of 0.01. Statistical significance was not found between 1 liter per minute ( $\underline{M}=4.36$ ,  $\underline{SE}=0.33$ ) and 2 liters per minute ( $\underline{M}=3.56$ ,  $\underline{SE}=0.22$ ) flow rates ( $\underline{M}$  difference =  $\pm 0.796$ ,  $\underline{SE} = 0.288$ ,  $p = 0.073$ ).

Data for gas analysis was collected at five minute intervals. Gas analysis included nitrogen, in addition to oxygen and argon. Data analysis for nitrogen is discussed under secondary findings. One-way repeated measures ANOVA showed statistically significant differences across flow rates for oxygen and argon concentrations. Pairwise comparisons determined which flow rates had the significant differences. Differences were seen between 0.5 liter and 1 liter, and 0.5 liter and 2 liters per minute flow rates. Significance was not found between 1 liter per minute and 2 liters per minute flow rate for oxygen or argon.

### Secondary Findings

Additional gas analysis of the inspired and expired gas concentrations, in a semi-closed anesthesia circle system, included nitrogen. This study found that oxygen dilution occurred as the argon concentration increased, but the investigators also found a corresponding increase in the nitrogen concentration. Table 6 compares the mean inspired concentration of nitrogen at the three different flow rates, with the mean inspired concentrations of oxygen and argon. The difference across flow rates in the inspired nitrogen concentration is seen at the 15 and 30 minute intervals. As flow rates decreased, nitrogen concentration increased over time at a higher rate than argon. The mean inspired nitrogen concentration for 2 liters per minute flow rate at baseline was 0.90 ( $\underline{SD}=1.24$ ), at 15 minutes it was 5.91% ( $\underline{SD}=5.93$ ), and at 30 minutes

Table 6

Mean Inspired Concentration of Oxygen, Argon, and Nitrogen at Baseline, 15 Minutes, and 30 Minutes

Flow Rate	Baseline		15 minutes		30 minutes	
	<u>M</u>	<u>SD</u>	<u>M</u>	<u>SD</u>	<u>M</u>	<u>SD</u>
2 L/min						
Oxygen	96.22	0.97	90.11	5.77	91.22	4.73
Argon	2.85	0.68	3.77	0.79	4.04	0.89
Nitrogen	0.90	1.24	5.91	5.93	4.58	4.90
1 L/min						
Oxygen	96.88	1.05	87.33	2.83	86.11	5.46
Argon	2.72	0.98	5.08	1.07	5.26	1.14
Nitrogen	0.39	0.15	7.23	2.01	8.26	4.84
0.5 L/min						
Oxygen	96.44	1.74	82.22	2.43	74.44	3.57
Argon	2.92	1.30	6.69	0.82	8.70	1.16
Nitrogen	0.61	0.66	10.70	2.36	16.44	3.04

Note. All above values are in percent.

it was 4.58% ( $SD=4.90$ ). The mean inspired nitrogen concentration for 1 liter per minute flow rate at baseline was 0.39 ( $SD=0.15$ ), at 15 minutes it was 7.23% ( $SD=2.01$ ), and at 30 minutes it was 8.26% ( $SD=4.84$ ). The mean inspired nitrogen concentration for 0.5 liter per minute flow rate at baseline was 0.61 ( $SD=0.66$ ), at 15 minutes it was 10.70% ( $SD=2.36$ ), and at 30 minutes it was 16.44% ( $SD=3.04$ ).

A statistically significant difference across flow rates in nitrogen accumulation was seen,  $F(2,16)=15.61$ ,  $p<0.0001$ ,  $\beta=0.997$ . Table 4 is revised to include nitrogen (Table 7) in addition to oxygen and argon. A statistically significant difference for time in nitrogen accumulation was also seen,  $F(2,16)=74.14$ ,  $p<0.0001$ ,  $\beta=1.000$ . Therefore, statistically significant differences were seen for inspired oxygen, argon, and nitrogen gas concentrations.

Table 7

Test of Within-Subjects Effects for Oxygen, Argon, and Nitrogen

Gas	Actual $F$ Value (Flow Rate)	Actual $F$ Value (Time)	Significance	Observed Power (Flow Rate/Time)
Oxygen	23.05	106.34	<.0001	1.000/1.000
Argon	21.71	119.67	<.0001	1.000/1.000
Nitrogen	15.61	74.14	<.0001	0.997/1.000

Note. Critical value of  $F=6.23$  (2,16 df);  $\alpha=0.01$ .

Using pairwise comparisons of three different flow rates for nitrogen concentration shows a statistically significant difference between 0.5 liter per minute ( $M=9.25$ ,  $SE=0.60$ ) and 1 liter per minute ( $M=5.29$ ,  $SE=0.74$ ) flow rates ( $M$  difference =  $\pm 3.959$ ,  $SE=0.822$ ,  $p=0.004$ ), and between 0.5 liter per minute ( $M=9.25$ ,  $SE=0.60$ ) and 2 liters per minute ( $M=3.80$ ,  $SE=1.32$ ) flow rates ( $M$  difference =  $\pm 5.456$ ,  $SE=1.242$ ,  $p=0.007$ ). It was not significant between 1 liter per minute ( $M=5.29$ ,  $SE=0.74$ ) and 2 liters per minute ( $M=3.80$ ,  $SE=1.32$ ) flow rates ( $M$  difference =  $\pm 1.496$ ,  $SE=0.914$ ,  $p=0.42$ ). Table 5 is revised to include nitrogen (Table 8) in addition to oxygen and argon.

Table 8

Pairwise Comparisons of Three Different Flow Rates for Oxygen, Argon, and Nitrogen

Flow rate comparison	Gas	Mean difference	Standard error	Significance
0.5 L/min:1 L/min <sup>†</sup>	Oxygen	±5.741	1.311	.007*
	Argon	±1.748	.536	.034
	Nitrogen	±3.959	.822	.004*
0.5 L/min:2 L/min <sup>†</sup>	Oxygen	±8.148	1.451	.002*
	Argon	±2.544	.314	.000*
	Nitrogen	±5.456	1.242	.007*
1 L/min:2 L/min <sup>†</sup>	Oxygen	±2.407	.858	.069
	Argon	±0.796	.288	.073
	Nitrogen	±1.496	.914	.420

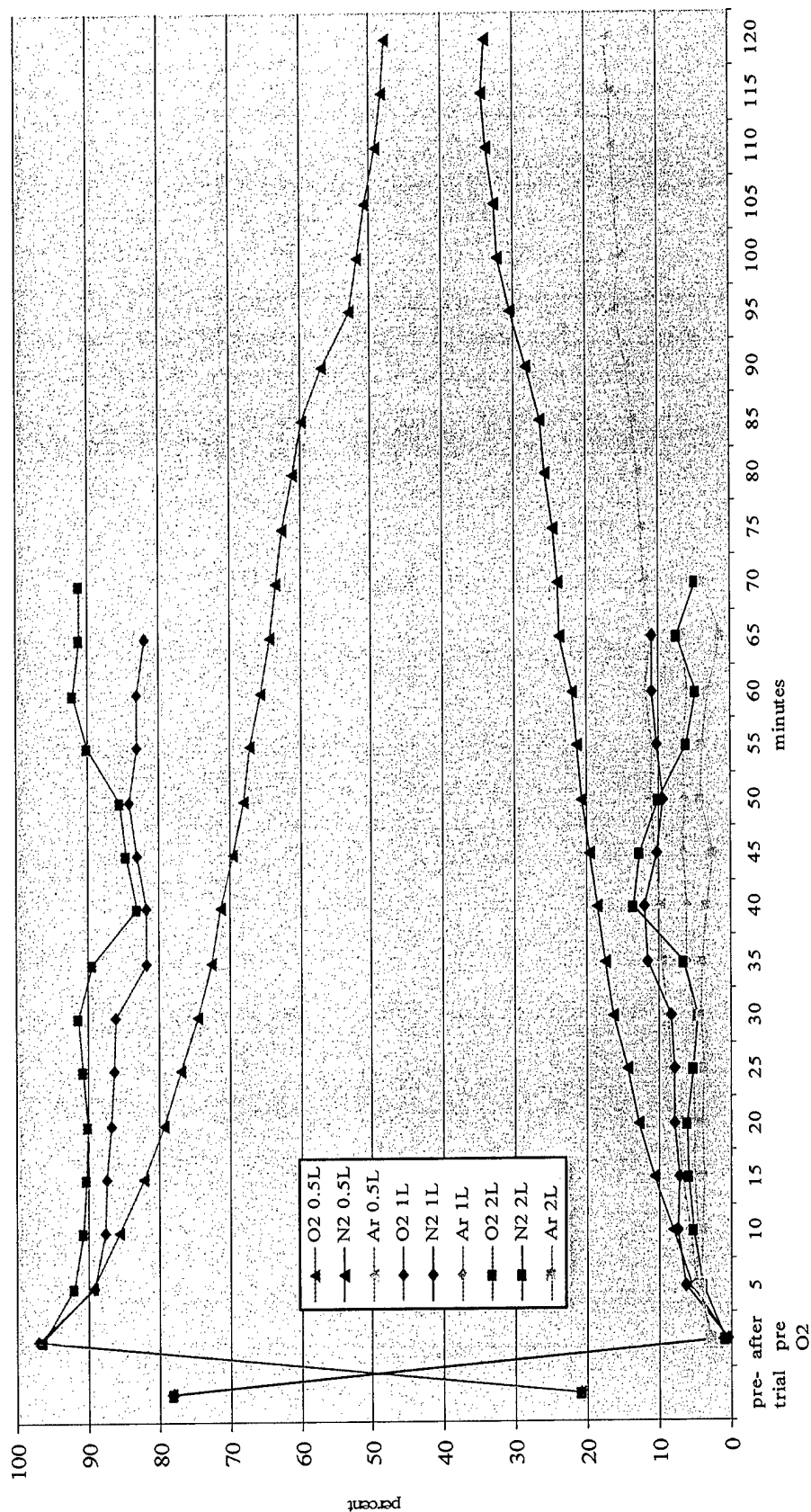
Note. \* Statistically significant at the 0.01 level. <sup>†</sup> Flow rate comparison was done in both directions.

### Summary

In summary, there were significant differences across flow rates in oxygen dilution, and argon and nitrogen accumulation using one-way repeated measures ANOVA. The means of the inspired concentration of oxygen, nitrogen and argon at all the data collection points are shown in Figure 3, refer to Table 2 for the number of subjects at each data collection point. Oxygen concentration decreased overtime, which was related to an increase in the amount of argon and nitrogen accumulation in the semi-closed anesthesia circle system. A higher amount of argon and nitrogen accumulation, resulting in a corresponding decrease in oxygen concentration was seen at the lowest flow rate (0.5 liter per minute).

A statistical significant difference in oxygen and nitrogen concentrations was noted between 0.5 liter per minute and 1 liter per minute, and an acknowledged difference for argon concentration. There is a statistically significant differences for oxygen, nitrogen, and argon between 0.5 liter per minute and 2 liter per minute. There is no significant difference for oxygen, nitrogen, or argon between 1 liter per minute and 2 liter per minute flow rates. In conclusion, the hypothesis was accepted and supported statistically.

Figure 3. Means of Inspired Concentrations of Oxygen ( $O_2$ ), Nitrogen ( $N_2$ ), and Argon (Ar) at all Data Collection Points.



## CHAPTER V

### Discussion, Conclusions, Implications, and Recommendations

Oxygen concentrators produce an unlimited supply of oxygen, which solves the logistical problems associated with deployed oxygen supplies and replaces compressed oxygen cylinders. Oxygen concentrators are used in field military hospitals, and are specifically used with the draw-over anesthesia system. Low flow anesthesia (less than 3 liters per minute) is a popular technique used to conserve resources (Cotter et al, 1991; Miller, 2000). This study, however, was designed to provide data for a minimal safe flow rate with a semi-closed anesthesia circle system using an oxygen concentrator as the fresh gas source.

Parker and Snowdon (1988) determined that fresh gas flows needed to be more than twice the patient's oxygen consumption so that argon accumulation would not be a significant issue. This study selected the three fresh gas flow rates (0.5 liter, 1 liter, 2 liters) based on the results from Parker and Snowdon's study. One of the problems encountered by Parker and Snowdon was the dilution of oxygen as argon accumulated within a semi-closed anesthesia circle system at low flow rates. Parker and Snowdon used a gas mixture of 90.5 % oxygen and 9.5% argon, in contrast this study used an oxygen concentrator as the oxygen source. The oxygen concentrator produced  $93\% \pm 3\%$  oxygen, with the remaining gas being argon and less than 1% nitrogen. Rathgeber et al. (1995) concluded, using a metabolic lung, that argon accumulation is flow rate dependent when using an oxygen concentrator for anesthesia. No studies were found that used an oxygen concentrator as the gas source to a semi-closed anesthesia circle system. This study therefore, provides new research in this area.

The purpose of this study was to determine the rate of oxygen dilution, resulting from argon accumulation, using three different low fresh gas flow rates ( 0.5 liter, 1 liter, and 2 liters per minute) from an oxygen concentrator in a semi-closed anesthesia circle system. In this chapter, the investigators interpret the findings as they relate to the research cited in the literature review. Dalton's Law of partial pressures was used as the theoretical framework, in that the pressure exerted by each individual gas in the gas mixture is independent of the pressures of the other gases (Levitzky, 1999). The hypothesis is explained in light of the theoretical framework. The investigators discuss strengths and weaknesses of the research

including limitations to the study. Finally, conclusions, implications, and recommendations for further research related to anesthesia practice are discussed.

## Discussion

### Conceptual Framework

According to Dalton's Law, the pressure exerted by each individual gas in a gas mixture is independent of the pressures of the other gases (Levitzky, 1999). In this study, the total alveolar pressure ( $P_A$ ) equals the partial pressures of water vapor ( $P_{H_2O}$ ), oxygen ( $P_{O_2}$ ), carbon dioxide ( $P_{CO_2}$ ), nitrogen ( $P_{N_2}$ ), and argon ( $P_{Ar}$ ) combined ( $P_A = P_{H_2O} + P_{O_2} + P_{CO_2} + P_{N_2} + P_{Ar}$ ). The actual volume of gases entering and leaving the alveoli per minute depends on the volume of the lungs, mechanics of the chest wall, the muscles of inspiration and expiration, and the rate of breathing.

The partial pressure gradient of each gas across the alveolar-capillary membrane influences the rate of diffusion. The alveolar partial pressure of each gas varies with inspiration and expiration. During inspiration, the partial pressure of the individual gas is related to the concentration of the inspired gases that are delivered to the lungs. On expiration, the concentration of the expired gases is dependent on the metabolic consumption of oxygen and production of carbon dioxide. The anesthetic gas monitor used in this study measured dry gases, in which the water vapor was removed from the analysis of the inspiratory and expiratory gases. This would result in the concentration of the gases being slightly higher. Using Dalton's Law, the total pressure of gases in the inspiratory limb includes oxygen, water vapor, argon, and nitrogen. During expiration, the total pressure of gases includes oxygen, carbon dioxide, water vapor, nitrogen, and argon.

As gases are exhaled into the expiratory limb, carbon dioxide was absorbed by the carbon dioxide absorber. Argon and nitrogen are not reabsorbed or metabolized by the body, so are returned to the inspiratory limb. Oxygen, that is not taken up by the blood and metabolized by the body, is exhaled into the expiratory limb and then joins the fresh gas flow that is supplied from the oxygen concentrator to the inspiratory limb. Any excess gas in the semi-closed circle system was removed by the APL valve. The APL valve was manually adjusted, by one of the investigators, to keep the reservoir bag from totally collapsing and possibly entraining room air into the circuit. The APL valve adjustment was based on the fresh gas

flow and the amount of excess gas in the circuit. The valve was almost closed with the lowest fresh gas flow (0.5 liter per minute), but there was no entrainment of room air observed during any of the trials.

Using Dalton's Law, the resulting partial pressure of each individual gas is directly related to its concentration. So the accumulation of nitrogen and argon within the circuit, and the corresponding increase in the inspiratory concentration of these gases, results in a decrease in the concentration and partial pressure of oxygen available for inspiration and alveolar diffusion. The conceptual framework is supported by the results of this study.

Hypothesis: There will be an increase in the rate of oxygen dilution, while remaining above an inspired oxygen concentration of 21%, by argon, as flow rates decrease in a semi-closed anesthesia circle system using an oxygen concentrator for the fresh gas source.

The oxygen concentrator used in this study was able to produce oxygen up to a rate of 3 liters per minute to the circuit, at an oxygen concentration of  $93\% \pm 3\%$ . The remaining gases included argon and a small amount of nitrogen. The concentration of the oxygen produced by the oxygen concentrator was sampled and recorded every 5 minutes during each trial. This sample was obtained prior to the gas mixture entering the semi-closed anesthesia circle system. The oxygen delivered to the semi-closed anesthesia circle system from the oxygen concentrator was a mean of 95.9% during the 2 liters per minute flow rate, 94.8% during the 1 liter per minute flow rate, and 93.1% for the 0.5 liter per minute flow rate. It was expected that the oxygen produced by the concentrator would normally vary but remain within the  $93\% \pm 3\%$  range, which it did.

The first data collection point was the baseline or zero minutes. The baseline reading was after the 10 minute preoxygenation and denitrogenation period, and was the start of the trial. The preoxygenation and denitrogenation was accomplished by an oxygen cylinder that was filled with a gas mixture produced by the oxygen concentrator. The oxygen concentrator produces a gas mixture of a normal variation in oxygen concentration ( $93\% \pm 3\%$ ), with the remaining gas being argon and less than 1% nitrogen. In this study, the baseline mean inspired oxygen was 96.22% at 2 liters per minute flow rate, 96.88% at 1 liter per minute flow rate, and 96.44% at 0.5 liter per minute flow rate. This slight variation of the mean inspired oxygen at

baseline across different flow rates may be due to the expected variation in the oxygen concentration produced by the oxygen concentrator.

Differences in the inspired oxygen and argon concentrations were seen between baseline, 15, and 30 minute intervals (Table 3) for each of the flow rates. From baseline to 30 minutes, at 2 liters per minute flow rate, there was a small decrease in the mean inspired oxygen (5%) and very small increase in argon concentration (1.19%). It should also be noted that a small increase in the mean inspired oxygen concentration was seen between 15 and 30 minutes (1.11%), not a decrease. This may be explained by the higher flow rate (2 liters per minute) which results in a faster achievement of an expired oxygen concentration plateau. There is also the variation in the amount of oxygen produced by the oxygen concentrator that could account for this slight difference. The expected decrease over time in the inspired oxygen concentration and increase in the inspired argon concentration at 2 liters per minute flow rate was seen. This finding is consistent with results seen in Parker and Snowdon's (1988) study. At 2 liters per minute flow rate, the oxygen supply was much greater than the metabolic consumption of oxygen by the average healthy adult (3.4 milliliters per kilogram per minute). The 2 liter per minute flow rate plateau or trial termination occurred an average of 38.8 minutes with an average inspired oxygen concentration of 90.78% ( $SD=4.60$ ).

As expected, from baseline to 30 minutes, there was a small decrease in the mean inspired oxygen concentration (10.77%) at 1 liter per minute flow rate. There was a concurrent increase in the mean inspired concentration of argon (2.54%). At 30 minutes there was still a mean oxygen concentration of 86.11% or 861 ml of oxygen available on inspiration. So physiologically, the oxygen supply (861 ml) for the average healthy adult (70 kg), was still greater than the oxygen demand (238 ml) under normal metabolic requirements. The 1 liter per minute flow rate plateau or trial termination occurred an average of 41 minutes with an average inspired oxygen concentration of 86.77%. ( $SD=3.81$ ).

The mean inspired oxygen concentration for 0.5 liter per minute between baseline and 30 minutes decreased 20%, and the mean inspired argon concentration increased by 5.78% (or about 0.19% per minute). This increase was almost two times the initial argon concentration of 2.93%. This increase is almost double for what was observed at the 1 liter per minute flow rate. Although 30 minutes was used for

the final data collection point for comparison analysis, it should be noted that there was a greater variation among subjects at the 0.5 liter per minute flow rate in both the time of trial termination and the inspired oxygen concentration. The 0.5 liter per minute flow rate trial termination or plateau occurred an average of 97 minutes with a mean inspired oxygen concentration of 58% ( $SD=11.46$ ) at the trial termination. The greater variation seen with the 0.5 liter per minute flow rate among healthy, unanesthetized subjects does not reflect a safe predictable flow rate while using an oxygen concentrator. Therefore this study does not support the 0.5 liter per minute flow rate to be used with the oxygen concentrator using a semi-closed anesthesia circle system. Parker and Snowdon (1988) support the use of fresh oxygen flows of 0.5 liter per minute, in that serious argon accumulation does not occur if the fresh gas flow is about twice the oxygen consumption.

In the laboratory study by Parker and Snowdon (1988), the end-tidal argon concentration doubled in about 60 minutes when using the 0.5 liter per minute flow from the tank containing 9.5% argon. The Parker and Snowdon laboratory study used one trial in a healthy unanesthetized adult, and measured the end tidal concentrations at different flow rates (0.31 L, 0.5 L, 0.7 L, 0.9 L, and 2 L). The Parker and Snowdon clinical study measured end tidal oxygen concentration in five anesthetized healthy adults. The data from the clinical study showed a decrease in end tidal oxygen concentration between 3.8% and 5.1%, or a decrease in the oxygen fraction of 0.17% per minute. Parker and Snowdon did not address other gases in the clinical study.

Although Parker and Snowdon (1988), in both the laboratory and clinical studies, found a similar trend in the decrease in oxygen concentration and argon accumulation, there are significant differences in the methodologies between their two studies and this study. In their laboratory study with one subject, Parker and Snowdon used a cylinder of gas comprising of 90.5% oxygen and 9.5% argon, and measured the end tidal gas concentrations. The trend in oxygen dilution at the three fresh gas flow rates found in this study (0.5 L, 1 L, and 2 L per minute) was similar to what Parker and Snowdon observed. In the unanesthetized subject, Parker and Snowdon found an end tidal argon concentration of approximately 10% at 2 liters per minute, approximately 20% at 0.5 liter per minute, and approximately 40% at 0.31 liter per minute. Parker and Snowdon used a fresh gas mixture containing 9.5% argon in this laboratory study in

which they measured argon concentration until it stabilized, or for a maximum of 90 minutes. But the end tidal argon concentration doubled at the 0.5 liter per minute flow rate. They observed a corresponding decrease in oxygen concentration with the argon accumulation. Parker and Snowdon concluded that in a semi-closed anesthesia circle system the fresh gas flow should be twice the patient's oxygen consumption.

In this study, there was a statistical significant difference in the inspired oxygen concentration between the 0.5 liter per minute flow rate and the 1 liter per minute flow rate ( $p=0.007$ ); and between the 0.5 liter per minute flow rate and the 2 liters per minute flow rate ( $p=0.002$ ). For inspired argon concentration, there was a recognized difference between the 0.5 liter per minute and 1 liter per minute flow rates ( $p=0.034$ ), and a statistically significant difference between 0.5 liter per minute and 2 liters per minute flow rates ( $p<0.0001$ ). There was no significant difference for inspired oxygen or argon concentrations between 1 liter per minute and 2 liters per minute flow rates. These results support the recommendation to use no less than 1 liter per minute flow rate with the semi-closed circle system in healthy adults while using an oxygen concentrator as the source of oxygen.

The results also showed statistically significant differences across flow rates in oxygen dilution and in argon accumulation. Although the comparison of the 30 minute time interval was used between flow rates, it was expected and observed that oxygen dilution would continue over time, especially for the lowest flow rate (0.5 liter per minute). This is a significant concern if the inspired oxygen concentration in a semi-closed anesthesia circle system drops to a non-therapeutic or even a hypoxic level. Using Dalton's Law during anesthesia the addition of volatile anesthetics and/or nitrous oxide to the semi-closed anesthesia circle system would also displace the amount of oxygen available for inspiration. This would further increase the risk of developing a non-therapeutic or hypoxic gas mixture.

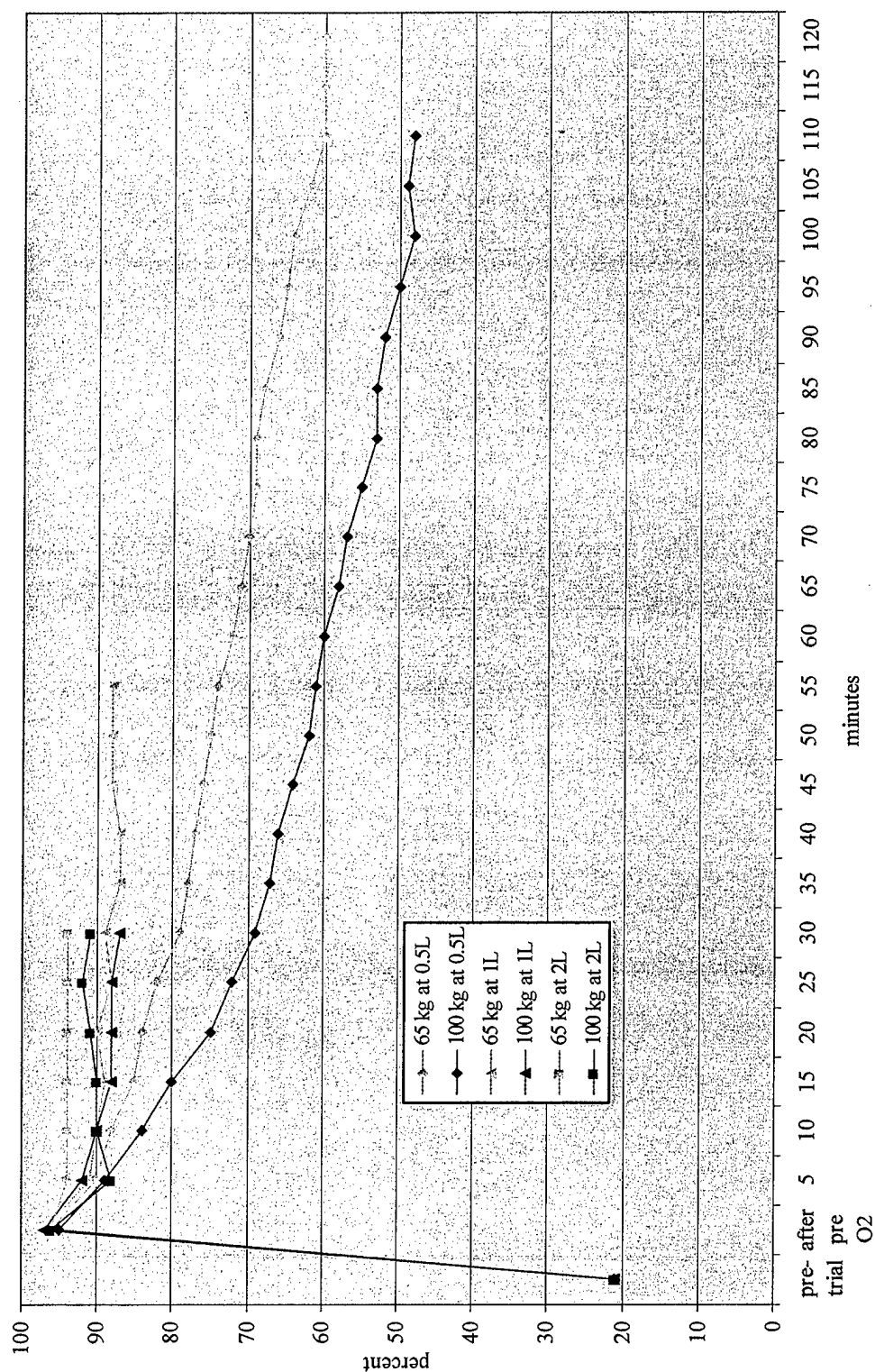
In contrast, the rate of oxygen dilution was not statistically significant between the 1 liter per minute and the 2 liters per minute flow rates. This can be explained by the metabolic consumption of oxygen by a healthy adult under normal circumstances. At 1 liter per minute flow rate, the amount of oxygen delivered to the subject was at least twice the metabolic consumption. For example, 86% (oxygen concentration) of 1000cc (flow rate) is 860cc. The metabolic rate of oxygen consumption for adults is approximately 3.4 milliliters per kilogram per minute under normal conditions (Levitzky, 1999). The mean weight for males

in this study was 84.8 kilograms, and the mean weight for females was 69 kilograms. Therefore the approximate metabolic rate of oxygen consumption per minute was 288.32 milliliters for males and 234.6 milliliters for females. The maximum weight of a subject in this study was 100 kilograms, or an oxygen consumption of 340 milliliters. So at 1 liter per minute, at about 86% oxygen concentration, the oxygen delivered (860 milliliters) to a 100 kg adult is still about two and a half times the estimated oxygen consumption (340 milliliters). This study supports that it would be safe to consider using an oxygen concentrator, with no less than a 1 liter per minute flow rate, with a semi-closed anesthesia circle system in healthy adults with normal metabolic oxygen requirements. This is safe as long as the amount of oxygen delivered (1 L) was at least twice the metabolic consumption of the adult.

During the practice of anesthesia, the anesthesia provider adjusts the amount of oxygen delivered (supply) to the patient's metabolic needs (demand). The metabolic rate for oxygen consumption will vary depending on weight, age, type of surgery/injury, activity, and temperature of the patient (Miller, 2000). The minute ventilation will increase under circumstances when the body requires a higher oxygen demand, this may be seen as an increase in tidal volume and/or an increase in respiratory rate (Levitzky, 1999). Rodgers, Tinker, Covino, & Longnecker (1993) state that the body's oxygen consumption is increased up to 25% postoperatively. There is also a two-to-five fold increase in oxygen consumption associated with shivering. They also discuss critical oxygen delivery, which is where the oxygen consumption level becomes supply dependent. At this point the oxygen delivery may need to be as high as 20 ml/kg/min to meet the demand of critically ill patients. Figure 4 shows the difference in the inspired oxygen concentration between a 65 kilogram and a 100 kilogram healthy adult subjects at three different flow rates. Healthy adults with normal metabolic requirements may have a flow rate of no less than 1 liter per minute from the oxygen concentrator. If the metabolic oxygen requirements increase at any time, then the anesthesia provider must adjust the flow rate from the oxygen concentrator to compensate for this change.

Metabolic oxygen consumption varies with age, weight, surgery/illness, activity, and temperature. The actual amount of oxygen metabolized varied with each individual, which accounts for the variation seen in the inspired oxygen concentrations for each flow rate. This is not normally measured in surgical

Figure 4: Comparison of Inspired Oxygen Concentration for a 65 kg Adult and a 100 kg Adult at 0.5 Liter, 1 Liter, and 2 Liters Flow Rates.



patients during anesthesia delivery. Anesthesia providers adjust the inspiratory oxygen based on the patient's overall health and response to anesthesia.

This study found that there was an increase in oxygen dilution as the flow rate was decreased from the oxygen concentrator in a semi-closed anesthesia circle system. At a flow rate of 0.5 liter per minute, it is possible the oxygen concentration in the semi-closed anesthesia circle system could theoretically fall below 21% oxygen, which could be fatal. The risk of this occurring would be greater if the circuit remained closed during the anesthetic delivery without periodic flushing of the anesthesia circle system. This is consistent with the research done by Parker and Snowdon (1988). Even with a baseline flow rate of 1 liter per minute, the anesthesia provider must still adjust the fresh gas flow rate from the oxygen concentrator based on the patient's estimated metabolic consumption of oxygen.

#### Additional Findings

Over time it was expected for each of the flow rates, while using a semi-closed anesthesia circle system, that the inspired oxygen concentration would decrease and the argon concentration would increase (Parker & Snowdon, 1988). Based on the results from Parker and Snowdon, it was expected to see a difference in inspired oxygen concentrations between the 0.5 liter per minute and the 2 liters per minute flow rate because of the differences in the oxygen supply compared to the metabolic oxygen consumption. It was expected that argon would accumulate leading to oxygen dilution at the lower flow rates, however, it was unexpected that nitrogen would accumulate significantly and attribute to the oxygen dilution. It was not known what to expect with the 1 liter per minute flow rate.

After preoxygenation and denitrogenation for 10 minutes, it was expected to have less than 1% concentration of nitrogen at baseline (Friesen, 1992). Most of the nitrogen from air is removed by the molecular sieve design of the oxygen concentrator while the oxygen is being concentrated, so there is usually less than 1% nitrogen remaining in the gas produced. At higher flow rates (starting about 4 liters) the concentration of oxygen produced will decrease as the molecular sieve removes less nitrogen (Harris & Stamp, 1987). Therefore, at 0.5 liter, 1 liter, and 2 liters flow rates, a nitrogen accumulation after a 10 minute preoxygenation and denitrogenation was not expected.

An unexpected gradual increase in nitrogen accumulation over time was observed. A statistically significant difference in nitrogen concentrations across flow rates and time was found. The baseline mean inspired nitrogen concentration, after a preoxygenation and denitrogenation period of 10 minutes, was less than 1% for each flow rate. The oxygen concentrator produced a gas mixture that contained less than 1% nitrogen. At 2 liters per minute flow rate, over 30 minutes there was an increase of 3.68% in the mean inspired nitrogen concentration. At 1 liter per minute flow rate, over 30 minutes, there was an increase of 7.97% in the mean inspired nitrogen concentration. At 0.5 liter per minute flow rate, there was an increase of 15.83% in the mean inspired nitrogen concentration. Parker and Snowdon (1988) discussed an observed increase in nitrogen accumulation when a closed circuit was used at the 0.31 liter flow rate. The gas mixture used by Parker and Snowdon during this laboratory study was 90.5% oxygen and 9.5% argon, with no mention of nitrogen.

In addition, a statistically significant difference was observed with nitrogen accumulation across flow rates. There was a statistically significant difference between 0.5 liter per minute and 1 liter per minute flow rates ( $p=0.004$ ), and between 0.5 liter per minute and 2 liters per minute flow rates ( $p=0.007$ ). There was no significant difference for inspired nitrogen concentration between 1 liter per minute and 2 liters per minute flow rates.

Anesthesia providers commonly preoxygenate and denitrogenate using a conventional 3-5 minute period of 100% oxygen or a four breath technique (Barash et al., 1997). On advice and in consultation with clinical anesthesia providers, it was assumed that a 10 minute period of preoxygenation and denitrogenation would eliminate the nitrogen stores adequately in the adult lungs when using a gas mixture containing less than 1% nitrogen. In this study, however, an increase in the inspiratory nitrogen concentration for all fresh gas flow rates was seen, with the highest concentration seen with the lowest gas flow (0.5 liter per minute). In fact, a mean increase in inspired nitrogen of about 15.83% (16.44% minus the baseline value of 0.61%) over the first 30 minutes at the 0.5 liter per minute flow rate was seen.

Thus it would appear that oxygen displacement is the result of not only argon but also nitrogen. Several research studies support this finding, but offer different explanations for nitrogen accumulation. This nitrogen accumulation, in addition to argon, resulted in displacing oxygen in the semi-closed

anesthesia circle system. The overall effect resulted in a decrease in the inspired oxygen concentration, which varied with the fresh gas flow rate. Nitrogen accumulation was observed in Parker and Snowdon's (1988) laboratory study. They observed an increase up to 9% in the end tidal nitrogen concentration, after 80 minutes at a fresh gas flow of 0.31 liter per minute. This occurred using a closed circuit on a healthy, unanesthetized adult. The authors did not discuss nitrogen concentration at any other flow rates, nor give any reason for this accumulation.

A review of the literature suggest differing mechanisms which may cause an increase in nitrogen. Barton and Nunn (1975) described an increase in the nitrogen concentration ranging from 3.5% to 15% as measured at the end of closed circuit anesthesia. They stated that the cause for the increase in nitrogen concentration to the normal body storage of nitrogen might be related to the effects of inadequate denitrogenation and/or the use of a closed circuit. During closed circuit anesthesia, which ranged from 34 to 135 minutes in length, an increase in the inspired nitrogen concentration was seen in all 16 subjects. Barton and Nunn stated that a more rapid increase in the inspired nitrogen concentration was seen with the subjects with the shortest denitrogenation periods. They also discussed that a supine 70 kg man contains about 2.7 liters of gaseous nitrogen; or 1.6 liters in the alveolar gas of the functional residual capacity, 0.55 liter in the water compartments of the body, and 0.55 liter in the fat compartments of the body. They, therefore, hypothesize that breathing oxygen at a rate of 10 liters per minute for 10 minutes may clear about 2 liters of nitrogen, the remaining 0.7 liter of nitrogen will gradually evolve into the gas space and accumulate in a closed circuit.

Johnson et al. (1979) discussed a "concentration effect" in which the rate of rise of the alveolar fraction of nitrous oxide is enhanced by an increase in the inspired concentration of nitrous oxide. They discussed the "second gas effect" in that there is a similar effect (increase) on the concentration of the second gas. Johnson et al. studied these effects in a closed system with a breath-holding maneuver using different nitrous oxide concentrations with argon and oxygen. They determined that with a high nitrous oxide technique, both alveolar concentrations of nitrous oxide and argon are concentrated. The increased concentration of argon in the lungs was because of an overall volume loss or an actual decrease in lung volume. This volume loss indicates that the volume of expiration is less than the volume of inspiration, and

that the gas components concentrate. Swanson, Johnson, & Virtue (1975) discussed the concentration effect of the insoluble gas argon when nitrous oxide was taken up into the blood in a closed glottis breath-hold. They described the uptake of nitrous oxide by the blood, which created a negative intrapulmonary pressure, so that the actual lung volume decreased. They hypothesize the same effect to occur with a semi-closed system. The uptake of oxygen at lower flow rates may concentrate the second gas (in this case, argon and nitrogen) indicating an overall volume loss (Miller, 2000). This may result in higher concentrations of the second gases in the expired gas concentrations, which may further increase after carbon dioxide is removed from the end tidal gas mixture. In contrast, a study done on the "second gas effect" found it not valid. Sun, Su, Shi, and Lee (1999) studied the effects of nitrous oxide and the ratio of the end tidal concentration to the inspired concentration of enflurane (second gas). They found that nitrous oxide did not effect the alveolar or blood concentration of enflurane, under constant volume ventilation, and that the "second gas effect" is not a valid concept.

The other possible explanation for the nitrogen accumulation after a 10 minute period of preoxygenation and denitrogenation is the volumes of distribution within the body. As discussed earlier, Barton and Nunn (1975) attempted to describe the effect of the water and fat body compartments on nitrogen in a closed system. Morita et al. (1985) discussed the rapid elimination rate of nitrogen from vessel rich tissues (such as heart, brain, kidney, and liver). But nitrogen that is stored in muscle, fat, and vessel poor tissues (such as cartilage and bone), have a lower elimination rate. Morita et al. stated that nitrogen from these tissues are still being eliminated in exhaled air after 30 minutes of breathing oxygen. This resulted in a nitrogen accumulation in a closed circuit.

So whether the nitrogen accumulation in this study was from the concentration effect/second gas effect or from the continued elimination from vessel poor tissue groups, or both, is not relevant for very small amounts of nitrogen. Room air normally contains about 78% nitrogen. The significance of nitrogen accumulation is that there is a displacement of the amount of available oxygen in a semi-closed anesthesia circle system. If the nitrogen and argon accumulation seen with the lowest fresh gas flow (0.5 liter per minute) goes undetected over a period of time, it may result in a hypoxic mixture since the amount of oxygen continually decreases in a linear fashion over time (Parker & Snowdon, 1988).

No other findings were associated with the subject's height, weight, age, sex, or BMI. Assessment data was only collected for monitoring the health of the subject during the trial, and no abnormal findings were seen. Metabolic consumption of oxygen in relation to the subject's body weight was discussed earlier.

In summary, it was found that oxygen dilution did occur due to argon and nitrogen accumulation at low flow rates using the oxygen concentrator as the fresh gas source in a semi-closed anesthesia circle system. The statistically significant difference seen in the 0.5 liter per minute flow rate is a cause of concern in a semi-closed circle system while using an oxygen concentrator. At 1 liter per minute and 2 liters per minute flow rate there was no significant differences. Parker and Snowden (1988) recommend that the inspired oxygen concentration remain more than twice the estimated metabolic oxygen demand. Therefore, we recommend that the lowest fresh gas flow rate that can be administered to healthy subjects at rest using an oxygen concentrator with a semi-closed anesthesia circle system, while remaining above an inspired oxygen concentration of 21%, is no less than 1 liter per minute fresh gas flow rate.

#### Study Strengths

There were several strengths of this research study. This study used the same subjects for each trial, which established a stronger comparison and less variability among the trials. This repeated measures design basically used each subject as their own control and provided the same physiological parameters during flow rate comparison. Another strength was the absence of attrition during the study. In addition, extraneous variables were minimized by the following ways. The same equipment and instrumentation were used for each trial, and there were no problems encountered with the equipment or instruments during the study either. The same investigators collected all the data and controlled the environment for extraneous variables that might impact the study. Data collection was done by the same investigators, in the same format each time, with the same instructions to each subject for each trial. The protocol was followed precisely during each trial, which strengthened the study and controlled for extraneous variables. Threats to internal and external validity were minimized by these study controls.

The results of this study demonstrate a significant difference in the inspiratory concentrations of oxygen, argon, and nitrogen over time while using an oxygen concentrator, with the largest difference seen with the lowest flow rate (0.5 liter per minute). These results support the existing literature and expands

upon the existing body of knowledge in the use of oxygen concentrators, specifically with the use of a semi-closed anesthesia circle system.

### Study Weaknesses

Several weaknesses of the study were identified which should be considered during data interpretation. These weaknesses include sample size, trial length, dry gas analysis, and physiological differences in the subject population. First, the use of convenience sampling limits the generalizability of the study results to the general population. All the subjects were Caucasian, which also limits the generalizability. The subject sample represents healthy adults of various ages, but there was an unequal number of male (five) and female (four) subjects. An alpha of 0.01 was used for statistical significance to give stronger results with this small sample size ( $n=9$ ).

Second, actual trial length varied between subjects and between flow rates. By establishing a minimum time for achieving a plateau and a maximum time for the completion of a trial, there was a wide range between these two points in the actual number of data collection points for each trial. This limited the data analysis in that the first 30 minutes was the only common time for all trials. Total number of subjects at the data collection points after 30 minutes varied; therefore data analysis was limited between subjects and between trials after 30 minutes.

Third, gas analysis was done on dry gases; therefore water vapor within the circuit was not accounted for. Although this is a common practice for gas analysis during anesthesia, it concentrates the gases slightly higher than actual values by removing the water vapor.

Fourth, measuring actual physiologic differences, specifically lung volumes and metabolic oxygen consumption, was not done. Metabolic consumption of oxygen varies based on the individual's physiological parameters and body requirements. Actual individual metabolic consumption of oxygen was not measured; neither were individual lung volumes. It was assumed that the variability seen among subjects in this study would reflect the variation seen in normal size adults.

A limitation to the use of the oxygen concentrator in anesthesia is the maximum liter flow of the oxygen concentrator and the current configuration of the oxygen concentrator. The oxygen concentrator is not designed to give a 10 liter flow to preoxygenate and denitrogenate prior to anesthesia. In this study, the

investigators used an oxygen cylinder, supplied with and filled by the oxygen concentrator, with a special adaptor to create the high 10 liter flow needed to accomplish preoxygenation and denitrogenation. The investigators then converted over directly to the oxygen concentrator without breaking the circuit. Currently, this technique would be difficult to duplicate in the field anesthesia environment, and standard oxygen tanks filled with compressed 100% oxygen would still be required for the standard anesthesia practice of preoxygenation and denitrogenation. There would also be a need to adapt the oxygen concentrator to provide fresh gas flow directly to an anesthesia machine. Current anesthesia machines have traditional connections for the compressed gas supply.

### Conclusions

In summary, this study found a statistically significant difference across flow rates in oxygen dilution by the accumulation of nitrogen and argon. Pairwise comparisons determined that there were significant differences between the 0.5 liter per minute and 1 liter per minute flow, and between the 0.5 liter per minute and 2 liters per minute flow rate. There were no significant differences between the 1 liter and 2 liters per minute flow rate. This study also demonstrated the unpredictability of the 0.5 liter per minute flow rate while using an oxygen concentrator in a semi-closed anesthesia circle system. The variation seen in the inspired oxygen concentration in healthy adults, and the overall decrease in the concentration overtime, leads to the conclusion that this could be an unsafe fresh gas flow rate with an oxygen concentrator in a semi-closed anesthesia circle system. The addition of other gases or volatile agents during anesthesia would also displace oxygen and decrease the oxygen concentration. Overall, there wasn't a significant difference between the 1 liter per minute flow rate and 2 liters per minute flow rate, while maintaining an inspired oxygen concentration (supply) more than twice the metabolic body requirements of oxygen (demand).

This study, therefore, recommends that no less than 1 liter per minute flow rate would be a safe minimum flow rate to use with the oxygen concentrator with a semi-closed anesthesia circle system in healthy adults, with normal metabolic oxygen requirements. Variations in metabolic oxygen consumption among individuals need to be assessed when deciding a fresh gas liter flow rate during the delivery of anesthesia. Individuals requiring an increase in minute ventilation, either by respiratory rate or tidal volume, may require an increase in the fresh gas flow rate from the oxygen concentrator. By

recommending a safe minimum flow rate to be used with the oxygen concentrator with a semi-closed anesthesia circle system, and by understanding the dilution of the oxygen concentration by the accumulation of argon and nitrogen over time, the anesthesia provider can maintain a therapeutic inspired oxygen concentration while providing a safe anesthetic.

#### Implications for Nursing Anesthesia Practice

The use of an oxygen concentrator during anesthesia in the field military environment provides a safe, cost effective supply of oxygen. By understanding the mechanics of an oxygen concentrator and how it produces oxygen, and the effects that a semi-closed anesthesia circle system has on the concentration of the inspiratory oxygen concentration, the anesthesia provider is able to adjust the fresh gas flow rate to compensate for the patient's metabolic needs. This study suggests a safe minimal flow rate of no less than 1 liter per minute to be used with the oxygen concentrator with a semi-closed anesthesia circle system in healthy adults.

Further development of a method to provide the regular fresh gas flow, and an 8-10 liter fresh gas flow for preoxygenation and denitrogenation, directly to the anesthesia machine from the oxygen concentrator is needed. This would enable the anesthesia provider to better utilize the oxygen concentrator, eliminate the need for a separate oxygen tank and adapter, and provide an easier transition to the lower desired fresh gas flow.

#### Recommendations for Further Research

This study could be repeated with a larger sample size. It is also recommended that pulmonary parameters be measured at the 1 liter fresh gas flow rate for 120 minutes, disregarding the achievement of a plateau. This would provide information based on tidal volume, metabolic oxygen consumption, and oxygen dilution while tightly controlling physiologic parameters. In addition, a study analyzing the inspired and expired gas concentrations during general anesthesia to healthy adults while using a 1 liter flow from the oxygen concentrator is recommended. This would provide the necessary data on further oxygen dilution with the addition of volatile anesthetics and/of nitrous oxide to the semi-closed anesthesia circle system.

Further research using the oxygen concentrator with a field anesthesia machine in a controlled environment, like the operating room, is recommended. Following this, a repeat study using the oxygen

concentrator during anesthesia in a field environment would be ideal. Studies using a field anesthesia machine, in which the oxygen concentrator is the oxygen source, would provide research directly applicable to providing anesthesia to patients in the field environment.

## APPENDIX A

Cole Parmer Flow Meter

**Litton**

**Life Support**

**Commercial Products**

P.O. Box 4508  
Davenport, Iowa  
52808-4508

Tel 319-383-6299  
Fax 319-383-6107

March 28, 2000

Col. Steve Janny

Steve,

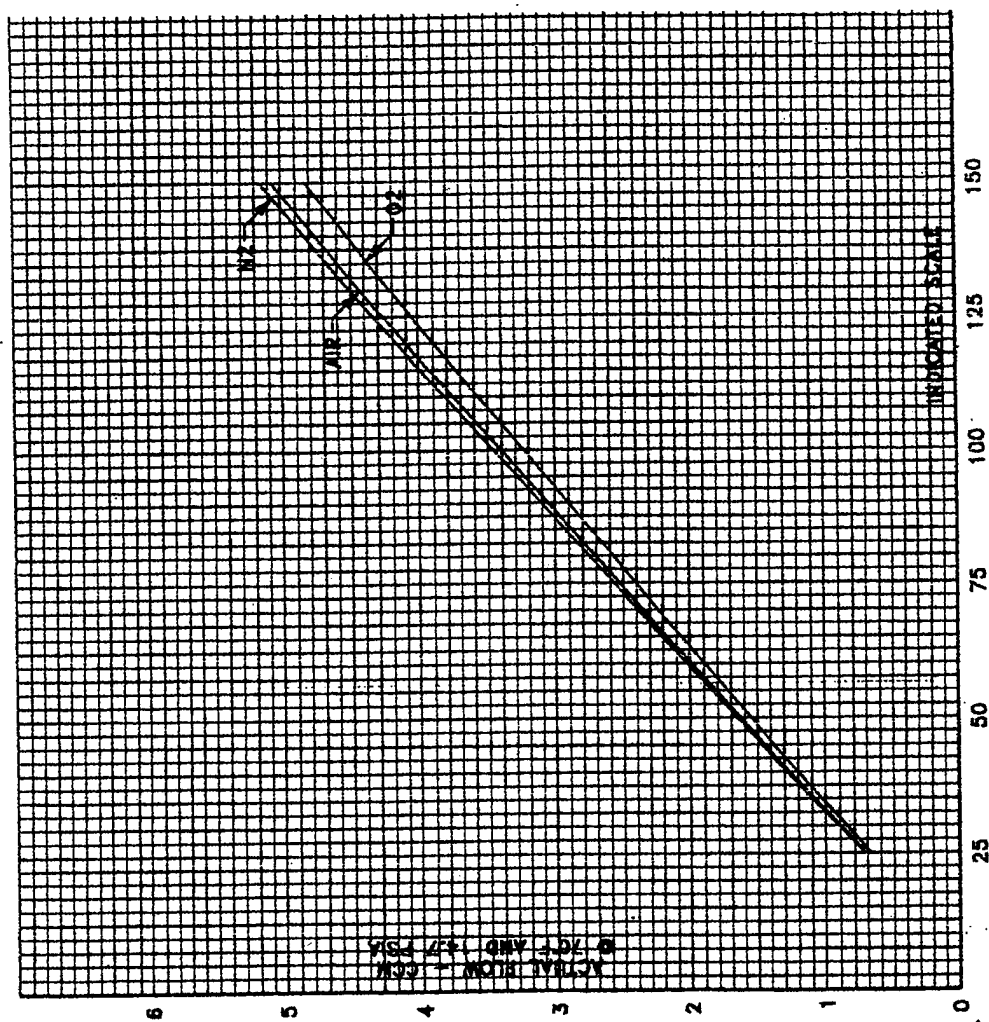
I have enclosed the two flowmeters that we talked about last Monday. The flow meters have calibration charts for air, nitrogen and oxygen. In your case the difference between 100% oxygen and 95% oxygen is going to be negligible so you can use oxygen curve. For indicated values below 25 with the Cole Parmer flowmeter the difference between air and oxygen is very small and you should be able to use the air values for a sapphire float given in the Cole Parmer calibration sheet with less than .05 lpm error. If you have any questions give me a call.

Sincerely,



Gary Byrd  
Engineering Manager  
Commercial Products Group  
Litton Life Support

## Cole Parmer Flow Meter Graph



## APPENDIX B

### Oxygen Concentrator's Cylinder Flow Calibration

## Oxygen Concentrator Tank Flow Letter

**Litton****Life Support**

Commercial Products  
P.O. Box 4508  
Davenport, Iowa  
52808-4508

Tel 319-383-6299  
Fax 319-383-6107

March 7, 2000

Col. Steve Jamny

Steve,

I have enclosed the two cylinders with modified pressure reducers that you requested. I have also included some test data that we ran on the reducers for your information. One of the reducers has a smaller reduced pressure range than other, 18.6 to 22.2 versus 22.4 to 28.6. This is probably because we used some engineering parts to build the reducers and the seat/ poppet combination on the one with a larger range isn't as good as it could be. The flow rates on both reducers are above 10 liters per minute when the cylinder pressure is above 300 psi with a maximum flow rate of 12 liters per minute at 2000 psi. You should expect the reducers to follow the curves shown with only small differences due to measurement and repeatability errors. If you have any problems with them let me know and I'll see what we can do to correct it. If you need anything else give me a call at 319-383-6299.

Sincerely,



Gary Byrd —  
Engineering Manager  
Commercial Products Group  
Litton Life Support

## APPENDIX C

Demographic and Health History Tool

## Demographic Data and Health History

Date \_\_\_\_\_

Subject # \_\_\_\_\_

Height \_\_\_\_\_ inches

Weight \_\_\_\_\_ pounds

Age \_\_\_\_\_

Sex \_\_\_\_\_

Medications: \_\_\_\_\_

Allergies: \_\_\_\_\_

Are you allergic to latex? \_\_\_\_\_

Do you smoke? \_\_\_\_\_

How much in the last year? \_\_\_\_\_

Are you pregnant? \_\_\_\_\_

Is there any possibility of being pregnant? \_\_\_\_\_

## History:

Have you ever had asthma? \_\_\_\_\_

Have you ever had COPD? \_\_\_\_\_

Have you had pneumonia in the last 6 months? \_\_\_\_\_

Have you had bronchitis in the last 6 months? \_\_\_\_\_

Have you had shortness of breath in the last 6 months? \_\_\_\_\_

Have you had difficulty breathing in the last 6 months? \_\_\_\_\_

Have you had a cold or flu in the last 6 weeks? \_\_\_\_\_

Have you ever had chest pain? \_\_\_\_\_

Have you ever had a heart attack? \_\_\_\_\_

Are you seeing a healthcare practitioner for anything? \_\_\_\_\_

Do you have any other medical history that relates to this study? \_\_\_\_\_

## Trial #1

Date \_\_\_\_\_

Is there any change in this information? \_\_\_\_\_

## Trial #2

Date \_\_\_\_\_

Is there any change in this information since your first trial? \_\_\_\_\_

## Trial #3

Date \_\_\_\_\_

Is there any change in this information since your second trial? \_\_\_\_\_

## APPENDIX D

Informed Consent

BROOKE ARMY MEDICAL CENTER/WILFORD HALL MEDICAL CENTER  
INFORMED CONSENT DOCUMENT  
(Revised: 19 Aug 99)

**Determination of the minimal fresh gas flow to maintain a therapeutic inspired oxygen level in a semi-closed anesthesia circle system using an oxygen concentrator as the oxygen source.**

You are being asked to participate in a research study. This research involves the use of an oxygen concentrator. The oxygen concentrator is a machine that removes most of the nitrogen from the air the patient is breathing. This leaves a gas mixture that is almost pure oxygen with some argon and nitrogen. All of these gases are harmless at these concentrations.

Usually, large heavy oxygen tanks are taken to the field when military hospitals accompany troops. The oxygen concentrator that will be used in this study is the same type that is being introduced to field military units. The purpose of this study is to find the lowest oxygen flow rate from the oxygen concentrator that keeps the amount of oxygen in your blood normal.

There is a risk of argon build up in the breathing circuit you are to breathe through, this may cause the oxygen concentration in this circuit to drop below 21%. This would be an unsafe oxygen concentration to breathe. This risk is minimal because oxygen and other gas concentrations are measured before and after you breathe. If the oxygen concentration you are to breathe drops below 21%, the trial is stopped.

This study will enroll nine (9) subjects at the Army Medical Department Center and School over a period of two weeks to three months.

You will be required to make three visits with the researchers during your participation. You have been asked to participate in this study because you are healthy and are not suffering from any disease or illness that may interfere with breathing.

**STUDY PARTICIPANTS:**

As a participant, you will participate in three different trials. Each trial will have a different flow rate of the gas mixture from the oxygen concentrator. The flow rate changes the amount of gas delivered each minute. You will not be told which flow rate is being used. Each trial will be a minimum of 30 minutes but will not be longer than 120 minutes.

**PROCEDURES:**

As a participant, you will undergo the following procedures:

Upon entering the study, you will be asked some questions regarding your health and life habits. Your height, weight, temperature, heart rate, blood pressure, and respiratory rate will be recorded. A clip will be placed on your finger, which will measure the amount of oxygen in your blood (oxygen saturation). You will be asked to drink, eat, and/or use the bathroom before the trial begins. During the trial, you will need to remain resting in one place. You will be able to communicate with the researchers at all times.

The amount of oxygen you breathe will always be more than the oxygen in the fresh air you normally breathe (21%). This study will be done in 3 stages using a different flow rate from the oxygen concentrator each time.

You will be positioned comfortably and begin breathing through a mask or mouthpiece that will be attached to the tubing (breathing circuit) and oxygen concentrator. The oxygen gas mixture will be on at this time so you may feel the flow of air on your face if you use a mask. At all times the oxygen gas mixture will be analyzed for oxygen content. The oxygen you inhale will never be less than what is in room air. Other gases in the circuit will be argon and nitrogen, which are harmless under these conditions. The concern is that argon may build up in the circuit and create an unsafe gas mixture. This risk is very small since the oxygen content is continuously checked and the trial will be stopped immediately if the oxygen content is below 21%.

Your heart rate, blood pressure, and oxygen saturation will be monitored throughout each trial. If there are any changes from initial measurements that may be of concern to your health, the trial will be stopped immediately. If there are any changes in the amount of oxygen in the breathing circuit that might be unsafe, the trial will be stopped immediately.

#### **RISKS OR DISCOMFORTS:**

The risks involved with this procedure are very small. If the amount of oxygen you breathe is ever less than 21%, the trial will stop and the mask or mouthpiece will be removed. If argon builds up in the circuit, such that the oxygen concentration falls below 21%, an unsafe gas mixture will result. If the unsafe gas mixture is not detected and the trial is not stopped immediately, serious injury from lack of oxygen to your brain and body may result which could even lead to death. This risk is small since there is continuous monitoring of the oxygen concentration you breathe by at least three different monitors, you are awake during each trial, and you will have your heart rate, blood pressure, and other physical signs monitored to prevent this from happening.

You will be breathing through a mask or mouthpiece for as long as the trial should last. You will not be able to eat, drink, or leave the room.

If for any reason you want to stop the trial you may.

As a FEMALE OF CHILDBEARING POTENTIAL wishing to volunteer for this project, you must understand that this study might be harmful to (1) an unborn child if you are pregnant or (2) an infant if you are breastfeeding. Therefore, to participate in this study, you cannot be pregnant. Any chance of pregnancy excludes you from the study. The effects of oxygen from an oxygen concentrator and of higher argon concentrations than you normally breathe on an unborn child are not known.

There may also be unforeseen risks associated with this study.

#### **BENEFITS:**

There is no guarantee you will receive any benefit from this study other than knowing that the information may help future patients.

#### **PAYMENT (COMPENSATION)**

You will not receive any compensation (payment) for participating in this study.

#### **ALTERNATIVE TREATMENT**

Choosing not to participate in this study is your alternative to volunteering for the study.

**CONFIDENTIALITY OF RECORDS OF STUDY PARTICIPATION:**

Records of participation in this study may only be disclosed in accordance with federal law, including the Federal Privacy Act, 5 U.S.C. 552a, and its implementing regulations. DD Form 2005, Privacy Act Statement-Health Care Records, contains the Privacy Act Statement for the records. By signing this document, you give your permission for information gained from your participation in this study to be published in medical literature, discussed for educational purposes, and used generally to further medical science. You will not be personally identified; all information will be presented as anonymous data.

Your records may be reviewed by the U.S. Food & Drug Administration (FDA), other government agencies, and/or the BAMC Institutional Review Boards.

Complete confidentiality cannot be promised, particularly for military personnel, because information regarding your health may be required to be reported to appropriate medical or command authorities.

**ENTITLEMENT TO CARE:**

Your entitlement to medical and dental care and/or compensation in the event of injury is governed by federal laws and regulations, and if you have questions about your rights or if you have received a research-related injury, you may contact the:

Brooke Army Medical Center Protocol Coordinators, 210-916-2598 or BAMC Judge Advocate, 210-916-2031.

Participation in this study does not alter your ongoing medical benefits as a military beneficiary, and you will continue to receive any needed medical treatment should you experience illness or injury as a result of this study. In the event of injury resulting from the investigational procedures, the extent of medical care provided is limited and will be within the scope authorized for DoD health care beneficiaries.

**STATEMENT OF GOOD FAITH:**

The investigators cannot guarantee or promise that you will receive benefits from this study; however, the investigators will keep you informed of any serious complications that may result from your participation in this study.

**VOLUNTARY PARTICIPATION:**

The decision to participate in this study is completely voluntary on your part. No one has coerced or intimidated you into participating in this project. You are participating because you want to. CPT Joan Grano or one of her associates has adequately answered any and all of your questions about this study, your participation, and the procedures involved. The principal investigator, CPT Grano (210) 930-6484, or a member of the Anesthesia Department staff (210) 221-6328 will be available to answer any questions concerning procedures throughout this study. If significant new findings develop during the course of this study that may relate to your decision to continue participation, you will be informed. You may withdraw this consent at any time and discontinue further participation in this study without affecting your eligibility for care or any other benefits to which you are entitled. Should you choose to withdraw, you must notify CPT Grano or one of her associates. You also understand that the investigator of this study may terminate your participation in this study at any time if she feels this to be in your best interest.

**AND**

You voluntarily consent to participate in this study. All oral and written information and discussions about this study have been in English, a language in which you are fluent.

A copy of this form has been given to you.

\_\_\_\_\_  
**VOLUNTEER'S SIGNATURE      VOLUNTEER'S SSN      DATE**

\_\_\_\_\_  
**VOLUNTEER'S PRINTED NAME**

\_\_\_\_\_  
**ADVISING INVESTIGATOR'S SIGNATURE      DATE      (PHONE #)**

\_\_\_\_\_  
**PRINTED NAME OF ADVISING INVESTIGATOR**

\_\_\_\_\_  
**WITNESS' SIGNATURE      DATE**  
(Must witness ALL signatures)

\_\_\_\_\_  
**PRINTED NAME OF WITNESS**

**TITLE OF STUDY:** Determination of the minimal fresh gas flow to maintain a therapeutic inspired oxygen level in a semi-closed anesthesia circle system using an oxygen concentrator as the oxygen source.

Protocol #:

Date Protocol Approved by WHMC/BAMC IRB:

Date(s) ICD Changes Approved by WHMC/BAMC IRB:

## APPENDIX E

Data Collection Tool

Subject #

Trial #

Date

void bladder

comfortable?

concentrator turned on but no flow

Rascal calibrated with 100% oxygen

Oximeter calibrated with 21% and 100% oxygen

STOP IF:

SaO2 &lt;

HR &lt; &gt;

BP &lt; &gt;

Time started

Temp

	pre-trial	after pre O2	10	20	30	40	50	60	70	80	90	100	110	120
FGF														
SpO2														
HR														
BP														
RR														

comments

time stopped

temp

Subject # \_\_\_\_\_  
 Trial # \_\_\_\_\_

	after pre O2	5	10	15	20	25	30	35	40	45	50	55
FGF	pre-trial											
FiO2 conc												
O2 insp												
N2 insp												
CO2 insp												
O2 exp												
N2 exp												
CO2 exp												

comments \_\_\_\_\_

	60	65	70	75	80	85	90	95	100	105	110	115	120
FGF													
FiO2 conc													
O2 insp													
N2 insp													
CO2 insp													
O2 exp													
N2 exp													
CO2 exp													

comments \_\_\_\_\_

## Data Collection Tool (page 3)

Subject #

Trial #	Time	Distance	Speed	Acceleration	Deceleration	Direction	Notes
1	0.00	0.00	0.00	0.00	0.00	North	
2	0.05	0.05	1.00	20.00	-20.00	North	
3	0.10	0.10	2.00	40.00	-40.00	North	
4	0.15	0.15	3.00	60.00	-60.00	North	
5	0.20	0.20	4.00	80.00	-80.00	North	
6	0.25	0.25	5.00	100.00	-100.00	North	
7	0.30	0.30	6.00	120.00	-120.00	North	
8	0.35	0.35	7.00	140.00	-140.00	North	
9	0.40	0.40	8.00	160.00	-160.00	North	
10	0.45	0.45	9.00	180.00	-180.00	North	
11	0.50	0.50	10.00	200.00	-200.00	North	
12	0.55	0.55	11.00	220.00	-220.00	North	
13	0.60	0.60	12.00	240.00	-240.00	North	
14	0.65	0.65	13.00	260.00	-260.00	North	
15	0.70	0.70	14.00	280.00	-280.00	North	
16	0.75	0.75	15.00	300.00	-300.00	North	
17	0.80	0.80	16.00	320.00	-320.00	North	
18	0.85	0.85	17.00	340.00	-340.00	North	
19	0.90	0.90	18.00	360.00	-360.00	North	
20	0.95	0.95	19.00	380.00	-380.00	North	
21	1.00	1.00	20.00	400.00	-400.00	North	
22	1.05	1.05	21.00	420.00	-420.00	North	
23	1.10	1.10	22.00	440.00	-440.00	North	
24	1.15	1.15	23.00	460.00	-460.00	North	
25	1.20	1.20	24.00	480.00	-480.00	North	
26	1.25	1.25	25.00	500.00	-500.00	North	
27	1.30	1.30	26.00	520.00	-520.00	North	
28	1.35	1.35	27.00	540.00	-540.00	North	
29	1.40	1.40	28.00	560.00	-560.00	North	
30	1.45	1.45	29.00	580.00	-580.00	North	
31	1.50	1.50	30.00	600.00	-600.00	North	
32	1.55	1.55	31.00	620.00	-620.00	North	
33	1.60	1.60	32.00	640.00	-640.00	North	
34	1.65	1.65	33.00	660.00	-660.00	North	
35	1.70	1.70	34.00	680.00	-680.00	North	
36	1.75	1.75	35.00	700.00	-700.00	North	
37	1.80	1.80	36.00	720.00	-720.00	North	
38	1.85	1.85	37.00	740.00	-740.00	North	
39	1.90	1.90	38.00	760.00	-760.00	North	
40	1.95	1.95	39.00	780.00	-780.00	North	
41	2.00	2.00	40.00	800.00	-800.00	North	
42	2.05	2.05	41.00	820.00	-820.00	North	
43	2.10	2.10	42.00	840.00	-840.00	North	
44	2.15	2.15	43.00	860.00	-860.00	North	
45	2.20	2.20	44.00	880.00	-880.00	North	
46	2.25	2.25	45.00	900.00	-900.00	North	
47	2.30	2.30	46.00	920.00	-920.00	North	
48	2.35	2.35	47.00	940.00	-940.00	North	
49	2.40	2.40	48.00	960.00	-960.00	North	
50	2.45	2.45					

FGF	1	2	3	4	5	6	7	8	9	10
O2 insp										
N2 insp										
O2 exp										
N2 exp										
comments										

### References

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## VITAE

Captain Joan Teresa Grano was born on 2 June 1959 in Boston, Massachusetts the daughter of John and Mary Cadigan. She graduated with honors from Woburn Senior High School in Massachusetts. She first attended Boston College until her move to Florida, where she received her Associate in Science and Associate in Arts degrees from St. Petersburg Junior College in 1981. In September 1981, she received her Florida registered nursing license and began working at Largo Medical Center Hospital, Florida. Her nursing career began on the neurology unit as a primary care nurse, then later transferred to the intensive care unit. In 1984, she received her Bachelor of Science degree with a major in nursing from the University of South Florida. She began working at Bay Pines VA Medical Center early 1985 in the medical intensive care unit. Late 1986, she completed a Master of Science degree with a major in Nursing from the University of South Florida, adult clinical nurse specialist. A short time later she took an advance nursing role as Infection Control Practitioner, which she continued in until March 1998. From 1991 until 1998, she was also an adjunct faculty member at St. Petersburg Junior College, and an officer in the United States Army Reserves. In 1998, she went on active duty in the Army as a commissioned officer in the Nurse Corps for enrollment in the U.S. Army Graduate Program in Anesthesia Nursing. She has two daughters, Rachel born in 1982 and Ashley born in 1987.

Captain Andrea Leigh Roberts was born in Greer, South Carolina on 28 December 1972. She is the daughter of Thomas and Linda Roberts. She attended West Florence High School in South Carolina and Delta High School in Alaska. She was involved in the Junior Reserve Officer Training Corps (JROTC), National Honor Society, cross country running, and student government. Her interest in the Army earned her a four year Reserve Officer Training Corps (ROTC) scholarship. She attended Seattle University in Washington. In June 1995, she earned a Baccalaureate of Science in Nursing and was commissioned a second lieutenant in the Army Nurse Corps. She went on active duty in August 1995, attended the AMEDD Officer Basic Course at Fort Sam Houston (FSH), Texas. Her first duty assignment was on the surgical ward at Tripler Army Medical Center in Hawaii. She completed the last year of her Hawaii assignment as the Head Nurse of the Ear, Nose, and Throat Clinic before leaving in March 1999. She then attended the Officer Advance Course at FSH, TX prior to enrollment in the U.S. Army Graduate Program in Anesthesia Nursing in June 1999. She has been married to Steven Schempp since 1996. Together, they have one son, Tyler born in 1998.

Captain Annabel Bigley was born in Manchester, England on 12 January 1963, the daughter of David and Shirley Shave. She graduated from Midlands Technical College in Columbia, South Carolina as a licensed practical nurse in 1988. She moved to Charlotte, North Carolina and worked in the Emergency Department at Carolina's Medical Center. In 1991, the American Red Cross employed her in the perioperative autologous services department. In 1993, she became charge nurse at Pro-Med minor emergency center. She received an Associate Degree with a Major in Nursing from Regents College in Albany, New York in 1994. In 1996, she graduated from Lenior-Rhyne College in Hickory, North Carolina with a Bachelor of Science in Nursing. She was then employed in the critical care area at Gaston Memorial Hospital and Cleveland Memorial Hospital. In 1999 she became a commissioned officer in the U.S. Army Nurse Corps, and attended the Officer Basic Course at FSH, Texas in March. In June, she entered the U.S. Army Graduate Program in Anesthesia Nursing. She has been married to Thomas Bigley since 1992.

This thesis was typed by the investigators.